

22

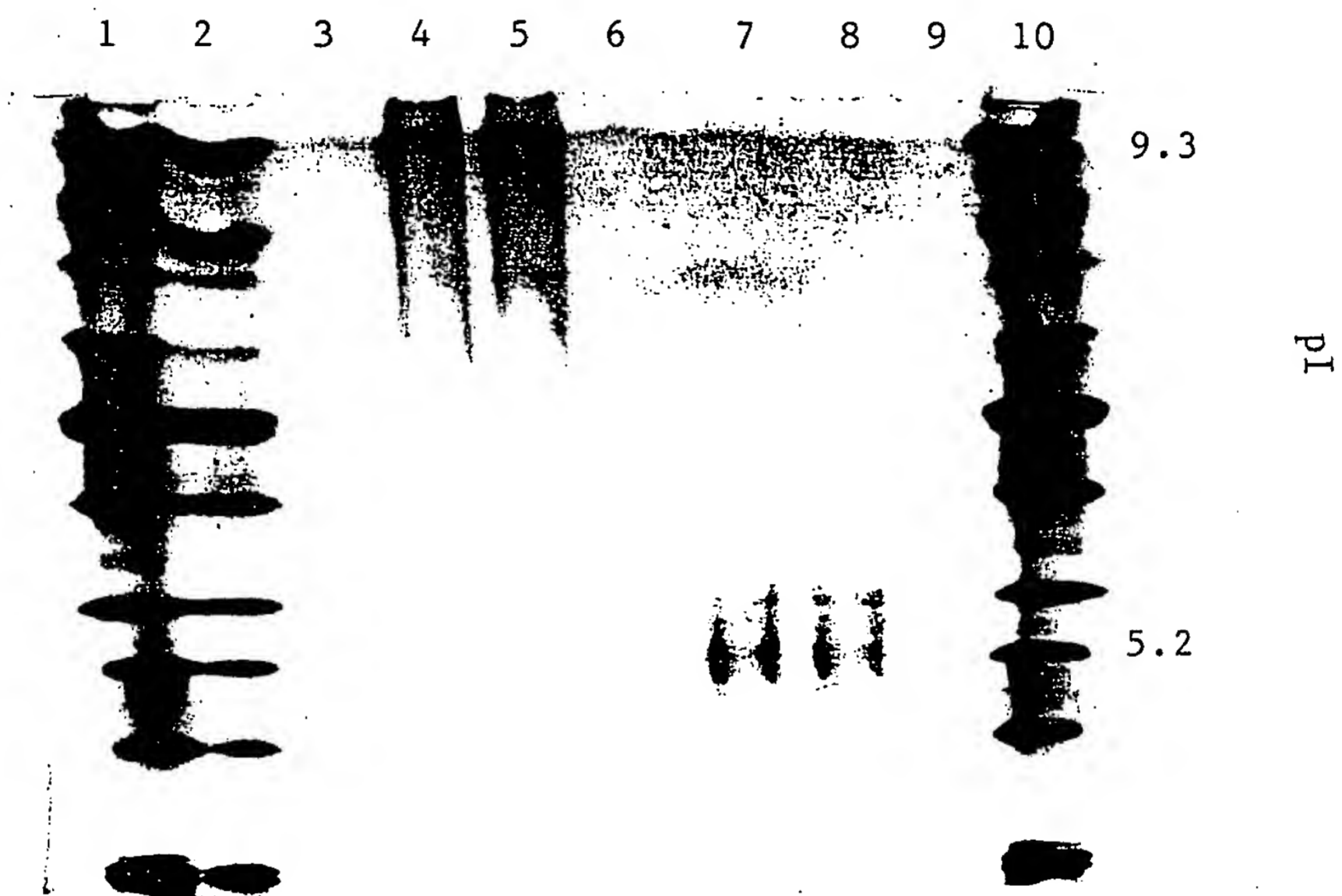


Figure 2

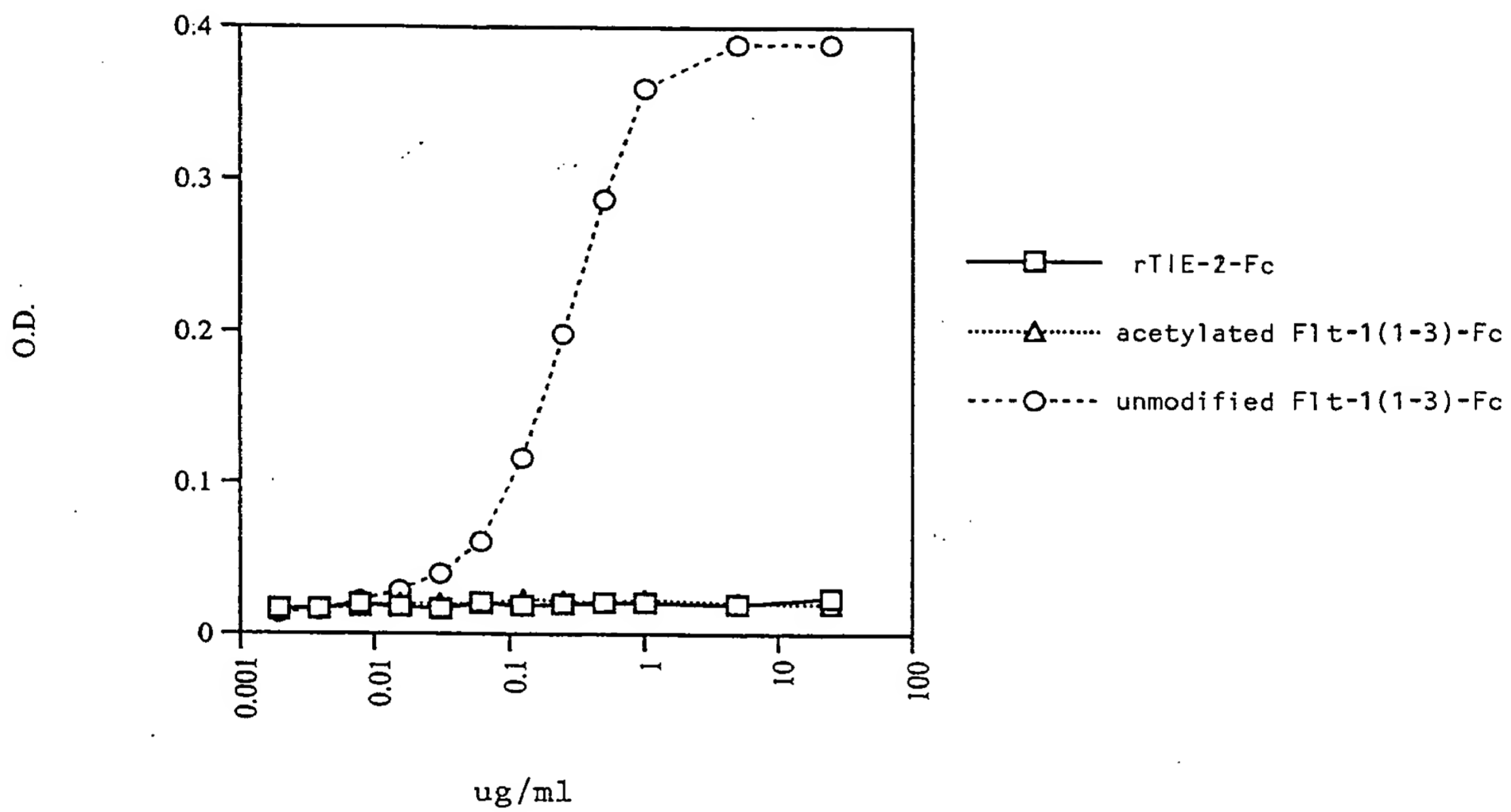


Figure 3

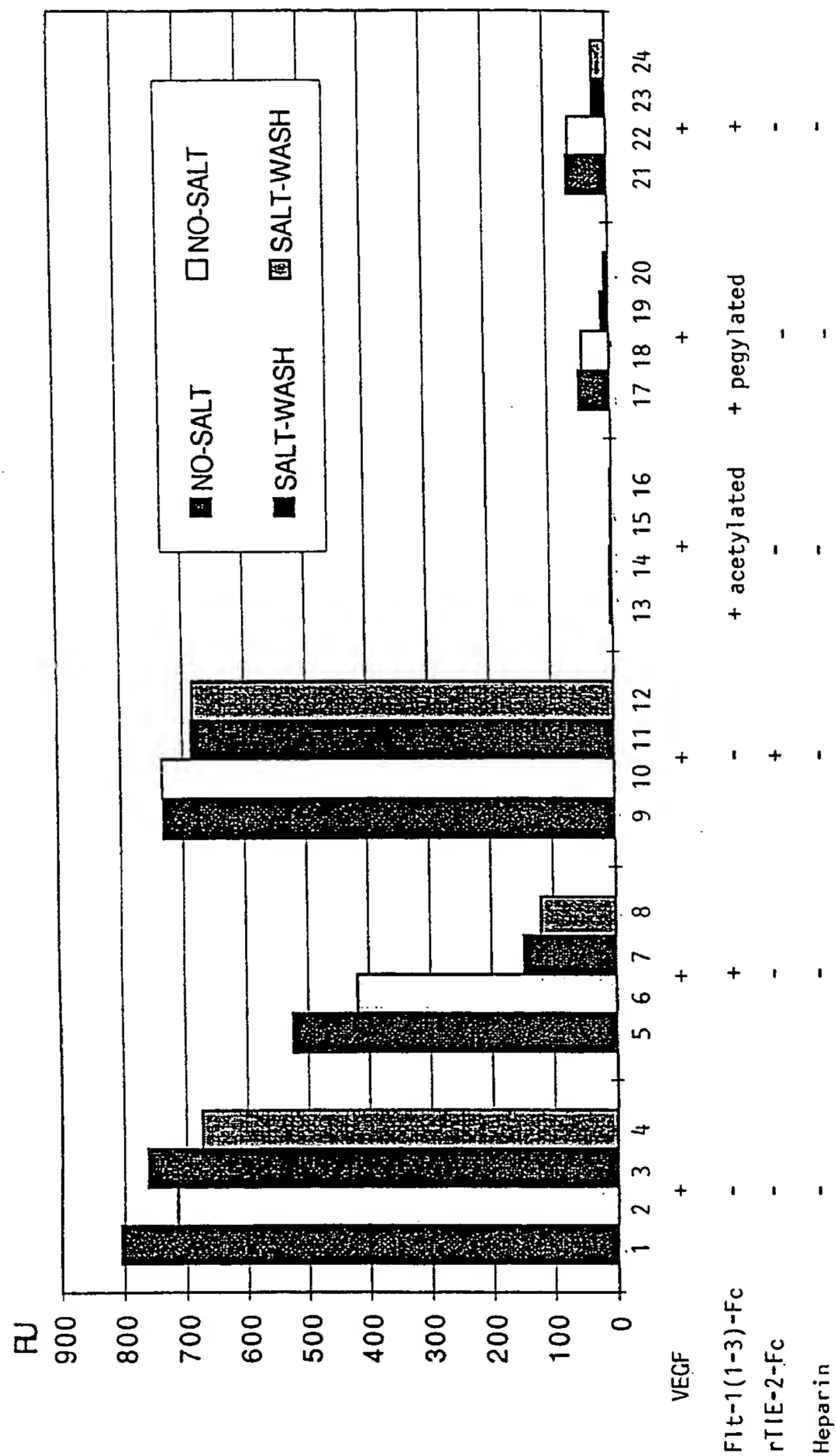


Figure 4

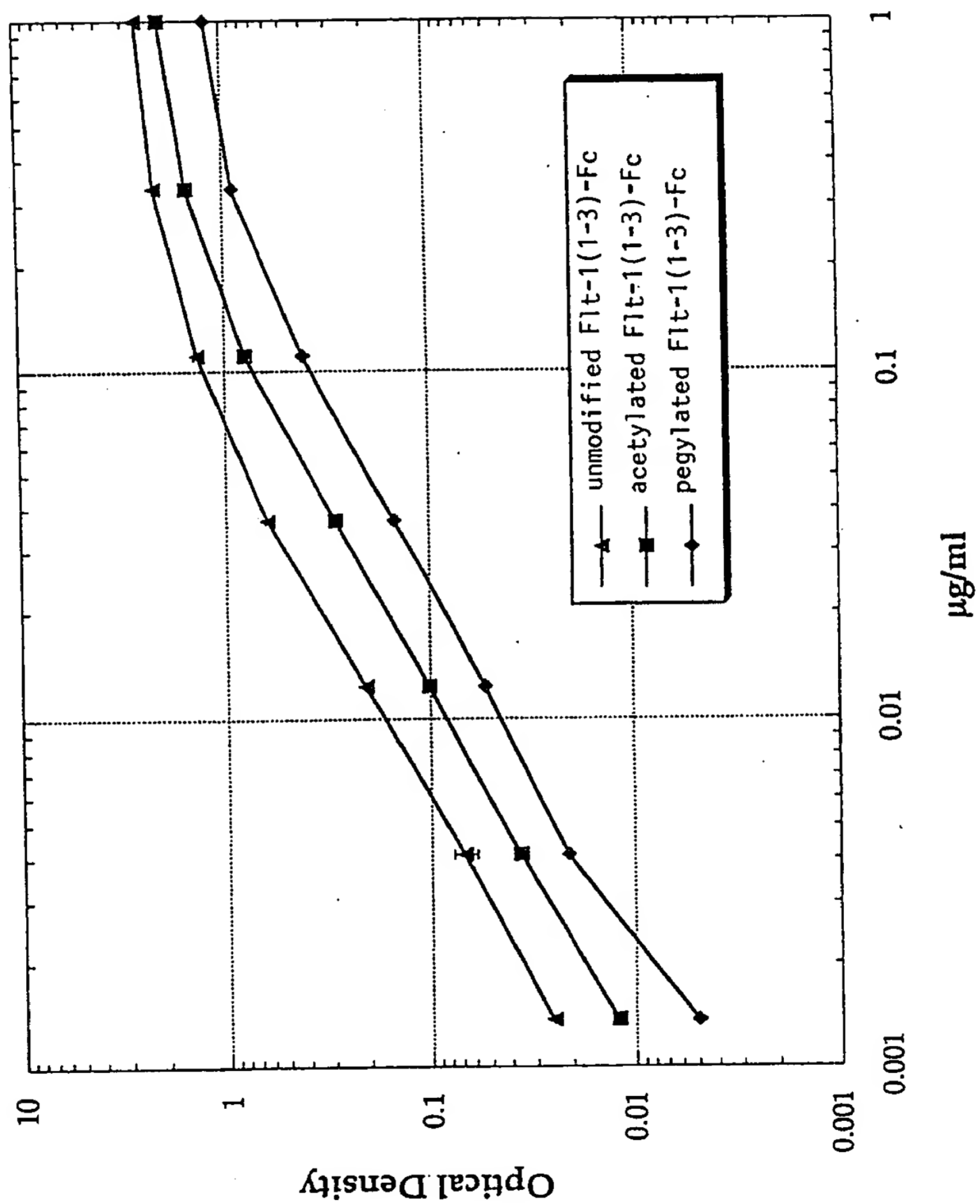
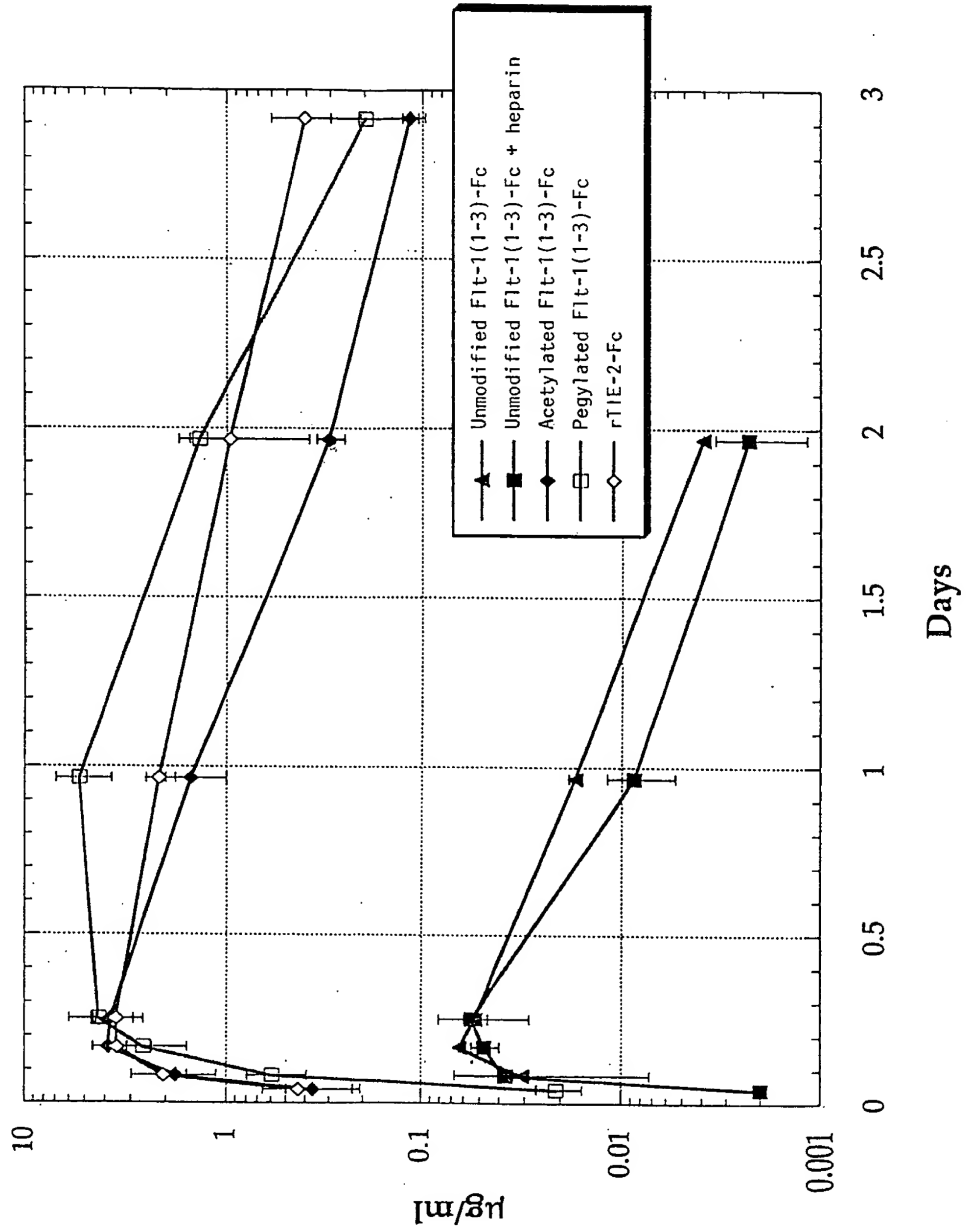


Figure 5



11 12 13 14 15 16 17 18 19 20

9.3
8.65
8.45
8.15
7.35
6.85
6.55
5.85
5.20
4.55
3.75
3.50

Figure 7

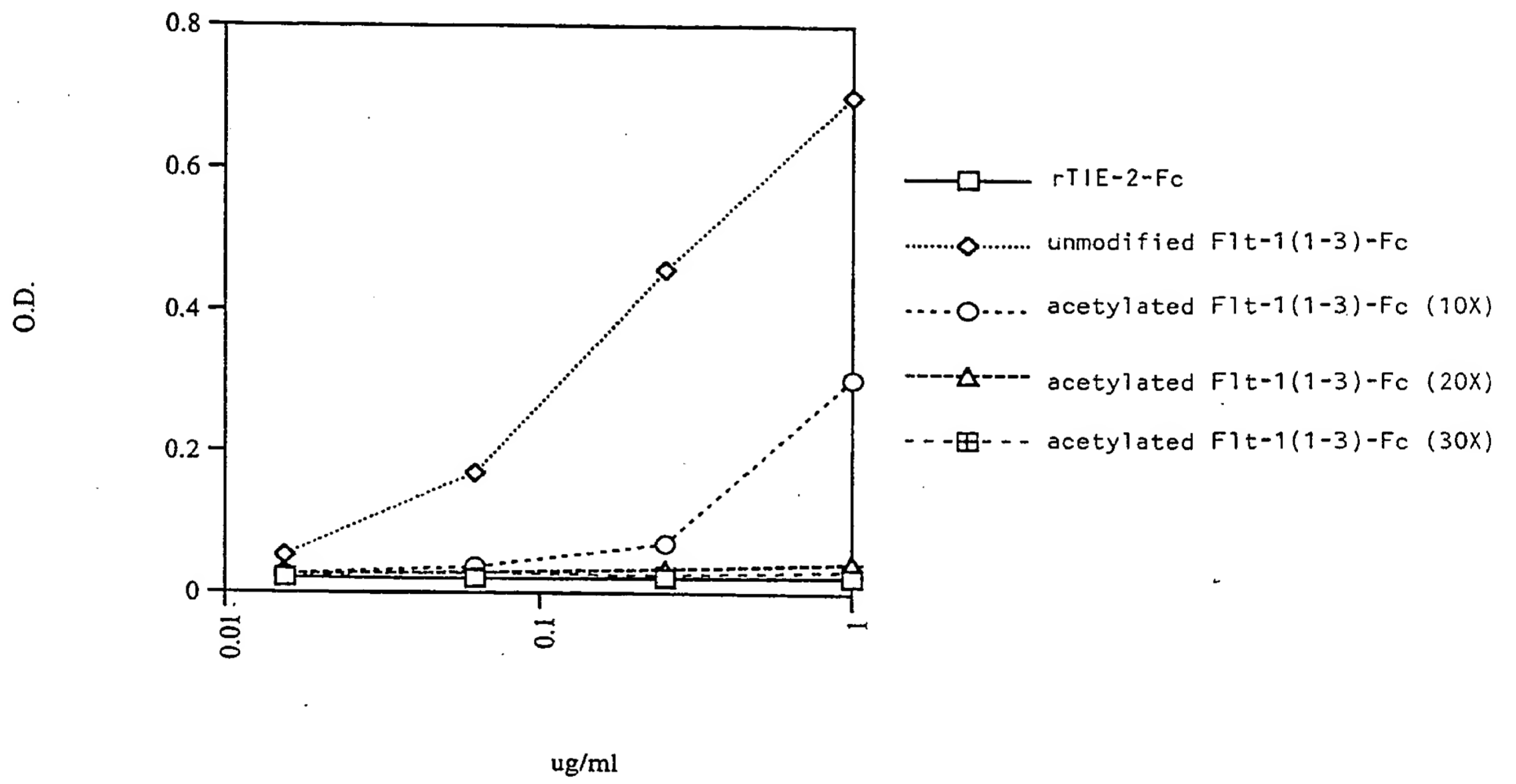
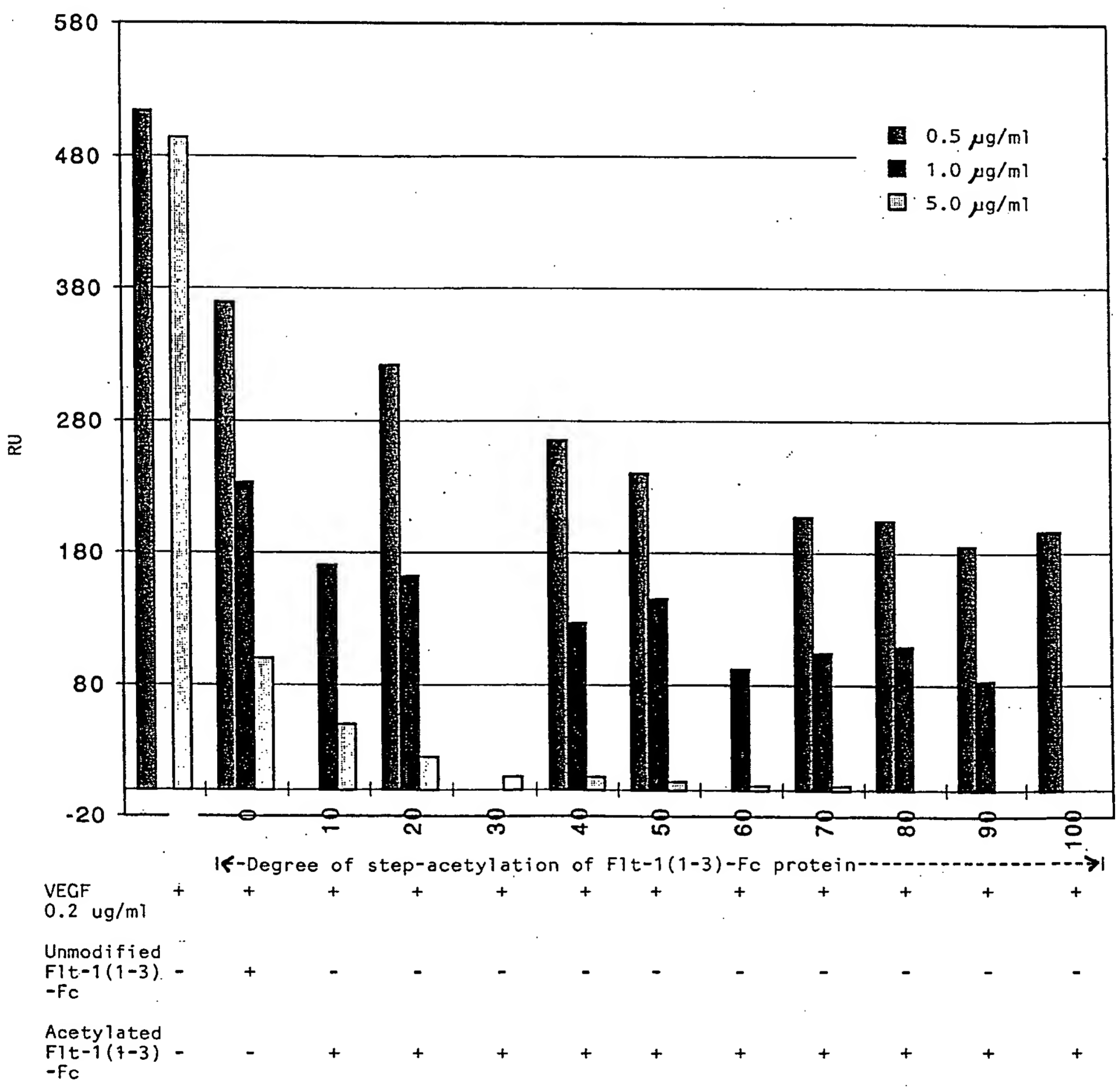


Figure 8

bioRxiv preprint doi: <https://doi.org/10.1101/2020.03.26.200720>; this version posted March 26, 2020. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.



SECRET

Figure 9

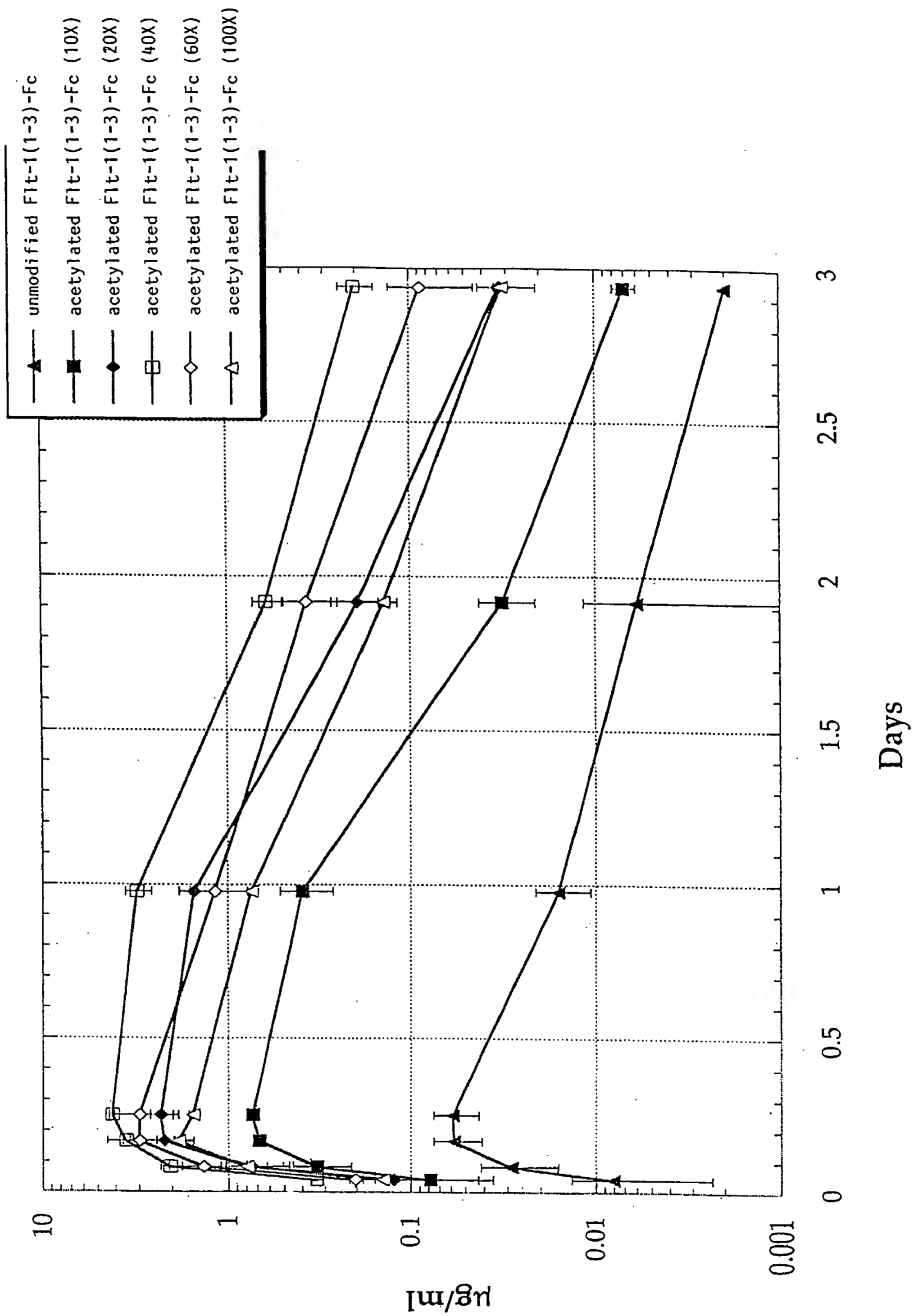


Figure 10A

10					20					30					40					50					60				
*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*									
ATG	GTC	AGC	TAC	TGG	GAC	ACC	GGG	GTC	CTG	CTG	TGC	GCG	CTG	CTC	AGC	TGT	CTG	CTT	CTC										
TAC	CAG	TCG	ATG	ACC	CTG	TGG	CCC	CAG	GAC	GAC	ACG	CGC	GAC	GAG	TCG	ACA	GAC	GAA	GAG										
Met	Val	Ser	Tyr	Trp	Asp	Thr	Gly	Val	Leu	Leu	Cys	Ala	Leu	Leu	Ser	Cys	Leu	Leu	Leu>										
70					80					90					100					110					120				
*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*										
ACA	GGA	TCT	AGT	TCA	GGT	TCA	AAA	TTA	AAA	GAT	CCT	GAA	CTG	AGT	TTA	AAA	GGC	ACC	CAG										
TGT	CCT	AGA	TCA	AGT	CCA	AGT	TTT	AAT	TTT	CTA	GGA	CTT	GAC	TCA	AAT	TTT	CCG	TGG	GTC										
Thr	Gly	Ser	Ser	Ser	Gly	Ser	Lys	Leu	Lys	Asp	Pro	Glu	Leu	Ser	Leu	Lys	Gly	Thr	Gln>										
130					140					150					160					170					180				
*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*										
CAC	ATC	ATG	CAA	GCA	GGC	CAG	ACA	CTG	CAT	CTC	CAA	TGC	AGG	GGG	GAA	GCA	GCC	CAT	AAA										
GTG	TAG	TAC	GTT	CGT	CCG	GTC	TGT	GAC	GTA	GAG	GTT	ACG	TCC	CCC	CTT	CGT	CGG	GTA	TTT										
His	Ile	Met	Gln	Ala	Gly	Gln	Thr	Leu	His	Leu	Gln	Cys	Arg	Gly	Glu	Ala	Ala	His	Lys>										
190					200					210					220					230					240				
*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*										
TGG	TCT	TTG	CCT	GAA	ATG	GTG	AGT	AAG	GAA	AGC	GAA	AGG	CTG	AGC	ATA	ACT	AAA	TCT	GCC										
ACC	AGA	AAC	GGA	CTT	TAC	CAC	TCA	TTC	CTT	TCG	CTT	TCC	GAC	TCG	TAT	TGA	TTT	AGA	CGG										
Trp	Ser	Leu	Pro	Glu	Met	Val	Ser	Lys	Glu	Ser	Glu	Arg	Leu	Ser	Ile	Thr	Lys	Ser	Ala>										
250					260					270					280					290					300				
*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*										
TGT	GGA	AGA	AAT	GGC	AAA	CAA	TTC	TGC	AGT	ACT	TTA	ACC	TTG	AAC	ACA	GCT	CAA	GCA	AAC										
ACA	CCT	TCT	TTA	CCG	TTT	GTT	AAG	ACG	TCA	TGA	AAT	TGG	AAC	TTG	TGT	CGA	GTT	CGT	TTG										
Cys	Gly	Arg	Asn	Gly	Lys	Gln	Phe	Cys	Ser	Thr	Leu	Thr	Leu	Asn	Thr	Ala	Gln	Ala	Asn>										
310					320					330					340					350					360				
*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*										
CAC	ACT	GGC	TTC	TAC	AGC	TGC	AAA	TAT	CTA	GCT	GTA	CCT	ACT	TCA	AAG	AAG	AAG	GAA	ACA										
GTG	TGA	CCG	AAG	ATG	TCG	ACG	TTT	ATA	GAT	CGA	CAT	GGA	TGA	AGT	TTC	TTC	TTC	CTT	TGT										
His	Thr	Gly	Phe	Tyr	Ser	Cys	Lys	Tyr	Leu	Ala	Val	Pro	Thr	Ser	Lys	Lys	Lys	Glu	Thr>										
370					380					390					400					410					420				
*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*										
GAA	TCT	GCA	ATC	TAT	ATA	TTT	ATT	AGT	GAT	ACA	GGT	AGA	CCT	TTC	GTA	GAG	ATG	TAC	AGT										
CTT	AGA	CGT	TAG	ATA	TAT	AAA	TAA	TCA	CTA	TGT	CCA	TCT	GGA	AAG	CAT	CTC	TAC	ATG	TCA										
Glu	Ser	Ala	Ile	Tyr	Ile	Phe	Ile	Ser	Asp	Thr	Gly	Arg	Pro</																

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Figure 10B

550	560	570	580	590	600
* * *	* * *	* * *	* * *	* * *	* * *
GGA AAA CGC ATA ATC TGG GAC AGT AGA AAG GGC TTC ATC ATA TCA AAT GCA ACG TAC AAA					
CCT TTT GCG TAT TAG ACC CTG TCA TCT TTC CCG AAG TAG TAT AGT TTA CGT TGC ATG TTT					
Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser Asn Ala Thr Tyr Lys>					
610	620	630	640	650	660
* * *	* * *	* * *	* * *	* * *	* * *
GAA ATA GGG CTT CTG ACC TGT GAA GCA ACA GTC AAT GGG CAT TTG TAT AAG ACA AAC TAT					
CTT TAT CCC GAA GAC TGG ACA CTT CGT TGT CAG TTA CCC GTA AAC ATA TTC TGT TTG ATA					
Glu Ile Gly Leu Leu Thr Cys Glu Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr>					
670	680	690	700	710	720
* * *	* * *	* * *	* * *	* * *	* * *
CTC ACA CAT CGA CAA ACC AAT ACA ATC ATA GAT GTC CAA ATA AGC ACA CCA CGC CCA GTC					
GAG TGT GTA GCT GTT TGG TTA TGT TAG TAT CTA CAG GTT TAT TCG TGT GGT GCG GGT CAG					
Leu Thr His Arg Gln Thr Asn Thr Ile Ile Asp Val Gln Ile Ser Thr Pro Arg Pro Val>					
730	740	750	760	770	780
* * *	* * *	* * *	* * *	* * *	* * *
AAA TTA CTT AGA GGC CAT ACT CTT GTC CTC AAT TGT ACT GCT ACC ACT CCC TTG AAC ACG					
TTT AAT GAA TCT CCG GTA TGA GAA CAG GAG TTA ACA TGA CGA TGG TGA GGG AAC TTG TGC					
Lys Leu Leu Arg Gly His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr Pro Leu Asn Thr>					
790	800	810	820	830	840
* * *	* * *	* * *	* * *	* * *	* * *
AGA GTT CAA ATG ACC TGG AGT TAC CCT GAT GAA AAA AAT AAG AGA GCT TCC GTA AGG CGA					
TCT CAA GTT TAC TGG ACC TCA ATG GGA CTA CTT TTT TTA TTC TCT CGA AGG CAT TCC GCT					
Arg Val Gln Met Thr Trp Ser Tyr Pro Asp Glu Lys Asn Lys Arg Ala Ser Val Arg Arg>					
850	860	870	880	890	900
* * *	* * *	* * *	* * *	* * *	* * *
CGA ATT GAC CAA AGC AAT TCC CAT GCC AAC ATA TTC TAC AGT GTT CTT ACT ATT GAC AAA					
GCT TAA CTG GTT TCG TTA AGG GTA CGG TTG TAT AAG ATG TCA CAA GAA TGA TAA CTG TTT					
Arg Ile Asp Gln Ser Asn Ser His Ala Asn Ile Phe Tyr Ser Val Leu Thr Ile Asp Lys>					
910	920	930	940	950	960
* * *	* * *	* * *	* * *	* * *	* * *
ATG CAG AAC AAA GAC AAA GGA CTT TAT ACT TGT CGT GTA AGG AGT GGA CCA TCA TTC AAA					
TAC GTC TTG TTT CTG TTT CCT GAA ATA TGA ACA GCA CAT TCC TCA CCT GGT AGT AAG TTT					
Met Gln Asn Lys Asp Lys Gly Leu Tyr Thr Cys Arg Val Arg Ser Gly Pro Ser Phe Lys>					
970	980	990	1000	1010	1020
* * *	* * *	* * *	* * *	* * *	* * *
TCT GTT AAC ACC TCA GTG CAT ATA TAT GAT AAA GCA GGC CCG GGC GAG CCC AAA TCT TGT					
AGA CAA TTG TGG AGT CAC GTA TAT ATA CTA TTT CGT CCG GGC CCG CTC GGG TTT AGA ACA					
Ser Val Asn Thr Ser Val His Ile Tyr Asp Lys Ala Gly Pro Gly Glu Pro Lys Ser Cys>					
1030	1040	1050	1060	1070	1080
* * *	* * *	* * *	* * *	* * *	* * *
GAC AAA ACT CAC ACA TGC CCA CCG TGC CCA GCA CCT GAA CTC CTG GGG GGA CCG TCA GTC					
CTG TTT TGA GTG TGT ACG GGT GGC ACG GGT CGT GGA CTT GAG GAC CCC CCT GGC AGT CAG					
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val>					

"TCT" 43453

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Figure 10C

1090	1100	1110	1120	1130	1140
* * *	* *	* *	* *	* *	* *
TTC CTC TTC CCC CCA AAA CCC AAG GAC ACC CTC ATG ATC TCC CGG ACC CCT GAG GTC ACA	AAG GAG AAG GGG GGT TTT GGG TTC CTG TGG GAG TAC TAG AGG GCC TGG GGA CTC CAG TGT	Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr>			
1150	1160	1170	1180	1190	1200
* * *	* *	* *	* *	* *	* *
TGC GTG GTG GTG GAC GTG AGC CAC GAA GAC CCT GAG GTC AAG TTC AAC TGG TAC GTG GAC	ACG CAC CAC CAC CTG CAC TCG GTG CTT CTG GGA CTC CAG TTC AAG TTG ACC ATG CAC CTG	Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp>			
1210	1220	1230	1240	1250	1260
* * *	* *	* *	* *	* *	* *
GGC GTG GAG GTG CAT AAT GCC AAG ACA AAG CCG CGG GAG GAG CAG TAC AAC AGC ACG TAC	CCG CAC CTC CAC GTA TTA CGG TTC TGT TTC GGC GCC CTC CTC GTC ATG TTG TCG TGC ATG	Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr>			
1270	1280	1290	1300	1310	1320
* * *	* *	* *	* *	* *	* *
CGT GTG GTC AGC GTC CTC ACC GTC CTG CAC CAG GAC TGG CTG AAT GGC AAG GAG TAC AAG	GCA CAC CAG TCG CAG GAG TGG CAG GAC GTG GTC CTG ACC GAC TTA CCG TTC CTC ATG TTC	Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys>			
1330	1340	1350	1360	1370	1380
* * *	* *	* *	* *	* *	* *
TGC AAG GTC TCC AAC AAA GCC CTC CCA GCC CCC ATC GAG AAA ACC ATC TCC AAA GCC AAA	ACG TTC CAG AGG TTG TTT CGG GAG GGT CGG GGG TAG CTC TTT TGG TAG AGG TTT CGG TTT	Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys>			
1390	1400	1410	1420	1430	1440
* * *	* *	* *	* *	* *	* *
GGG CAG CCC CGA GAA CCA CAG GTG TAC ACC CTG CCC CCA TCC CGG GAT GAG CTG ACC AAG	CCC GTC GGG GCT CTT GGT GTC CAC ATG TGG GAC GGG GGT AGG GCC CTA CTC GAC TGG TTC	Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys>			
1450	1460	1470	1480	1490	1500
* * *	* *	* *	* *	* *	* *
AAC CAG GTC AGC CTG ACC TGC CTG GTC AAA GGC TTC TAT CCC AGC GAC ATC GCC GTG GAG	TTG GTC CAG TCG GAC TGG ACG GAC CAG TTT CCG AAG ATA GGG TCG CTG TAG CGG CAC CTC	Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu>			
1510	1520	1530	1540	1550	1560
* * *	* *	* *	* *	* *	* *
TGG GAG AGC AAT GGG CAG CCG GAG AAC AAC TAC AAG ACC ACG CCT CCC GTG CTG GAC TCC	ACC CTC TCG TTA CCC GTC GGC CTC TTG TTG ATG TTC TGG TGC GGA GGG CAC GAC CTG AGG	Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser>			
1570	1580	1590	1600	1610	1620
* * *	* *	* *	* *	* *	* *
GAC GGC TCC TTC TTC CTC TAC AGC AAG CTC ACC GTG GAC AAG AGC AGG TGG CAG CAG GGG	CTG CCG AGG AAG AAG GAG ATG TCG TTC GAG TGG CAC CTG TTC TCG TCC ACC GTC GTC CCC	Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly>			

1090
 1100
 1110
 1120
 1130
 1140
 1150
 1160
 1170
 1180
 1190
 1200
 1210
 1220
 1230
 1240
 1250
 1260
 1270
 1280
 1290
 1300
 1310
 1320
 1330
 1340
 1350
 1360
 1370
 1380
 1390
 1400
 1410
 1420
 1430
 1440
 1450
 1460
 1470
 1480
 1490
 1500
 1510
 1520
 1530
 1540
 1550
 1560
 1570
 1580
 1590
 1600
 1610
 1620

Figure 10D

		1630			1640			1650			1660			1670			1680				
	*	*	*		*		*	*	*	*	*	*	*	*	*	*	*	*	*	*	
AAC	GTC	TTC	TCA	TGC	TCC	GTG	ATG	CAT	GAG	GCT	CTG	CAC	AAC	CAC	TAC	ACG	CAG	AAG	AGC		
TTG	CAG	AAG	AGT	ACG	AGG	CAC	TAC	GTA	CTC	CGA	GAC	GTG	TTG	GTG	ATG	TGC	GTC	TTC	TCG		
Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser>		

		1690			1700																
	*	*	*		*																
CTC	TCC	CTG	TCT	CCG	GGT	AAA	TGA														
GAG	AGG	GAC	AGA	GGC	CCA	TTT	ACT														
Leu	Ser	Leu	Ser	Pro	Gly	Lys	***>														

1630
 1640
 1650
 1660
 1670
 1680
 1690
 1700

Figure 11

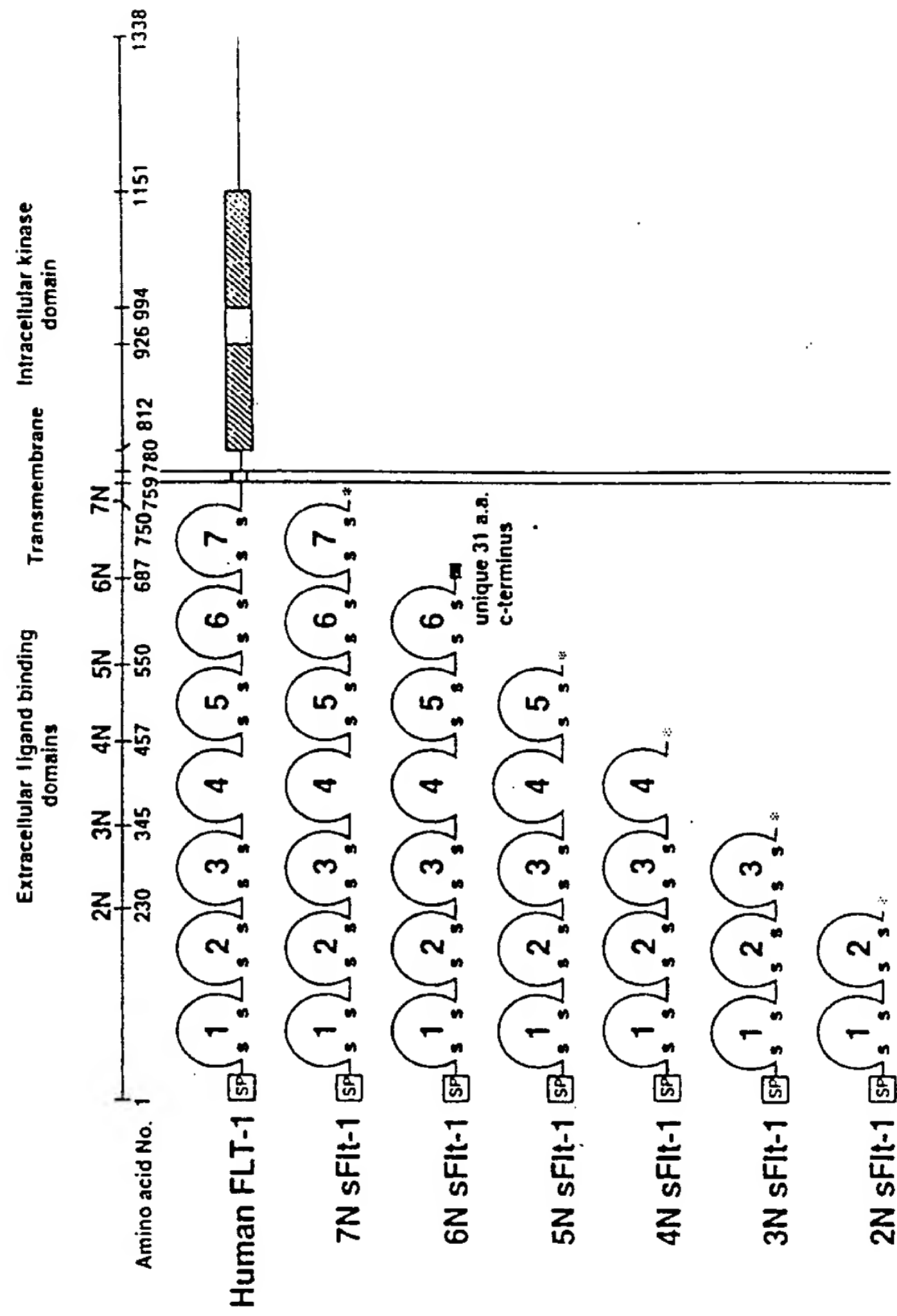


Figure 12A

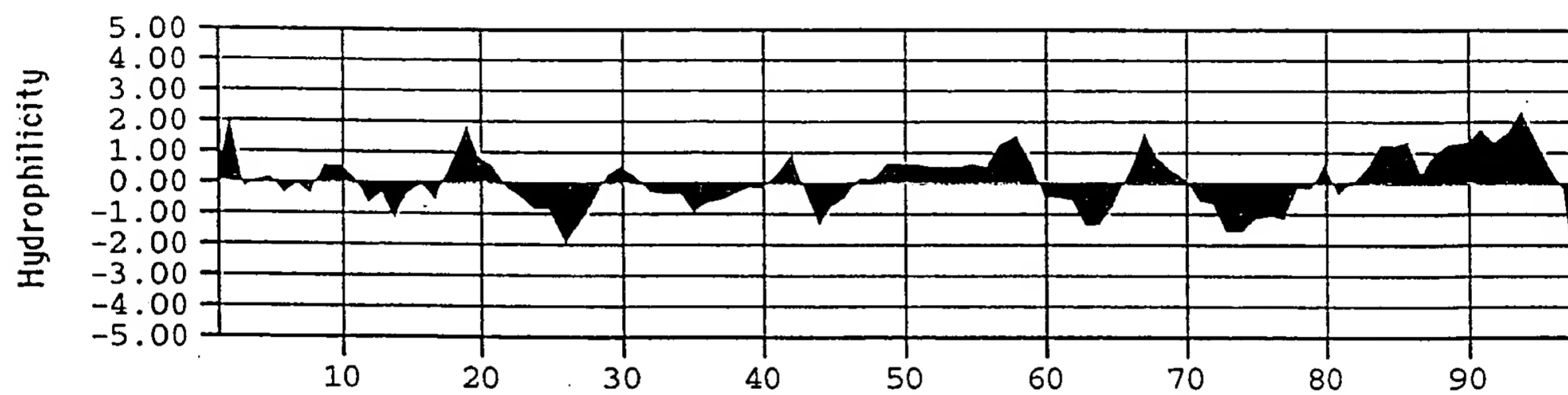


Figure 12B

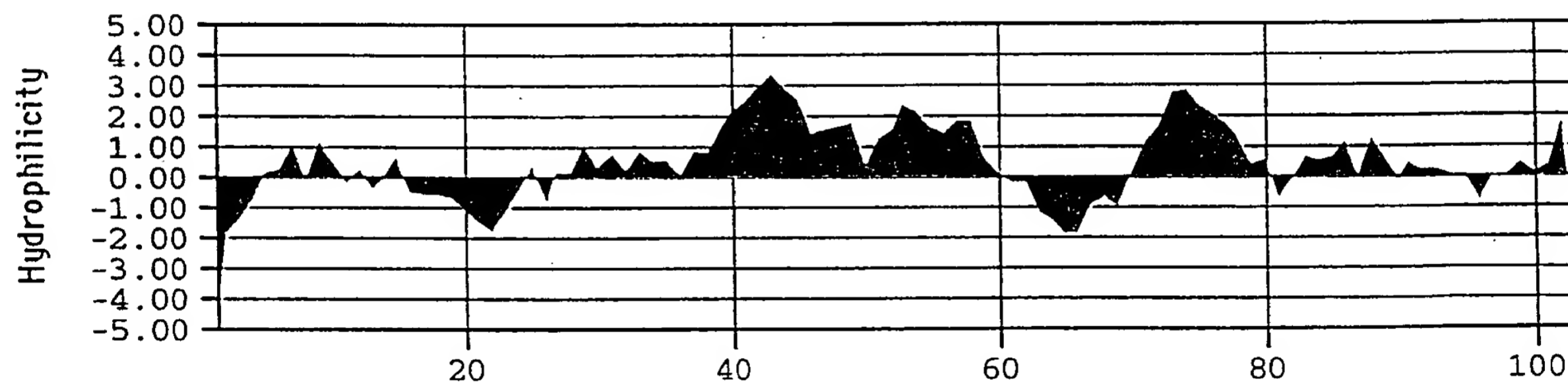


Figure 13A

```

      10      20      30      40      50      60
      *      *      *      *      *      *
ATG GTC AGC TAC TGG GAC ACC GGG GTC CTG CTG TGC GCG CTG CTC AGC TGT CTG CTT CTC
TAC CAG TCG ATG ACC CTG TGG CCC CAG GAC GAC ACG CGC GAC GAG TCG ACA GAC GAA GAG
Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser Cys Leu Leu Leu>

      70      80      90      100      110      120
      *      *      *      *      *      *
ACA GGA TCT AGT TCA GGT TCA AAA TTA AAA GAT CCT GAA CTG AGT TTA AAA GGC ACC CAG
TGT CCT AGA TCA AGT CCA AGT TTT AAT TTT CTA GGA CTT GAC TCA AAT TTT CCG TGG GTC
Thr Gly Ser Ser Ser Gly Ser Lys Leu Lys Asp Pro Glu Leu Ser Leu Lys Gly Thr Gln>

      130      140      150      160      170      180
      *      *      *      *      *      *
CAC ATC ATG CAA GCA GGC CAG ACA CTG CAT CTC CAA TGC AGG GGG GAA GCA GCC CAT AAA
GTG TAG TAC GTT CGT CCG GTC TGT GAC GTA GAG GTT ACG TCC CCC CTT CGT CGG GTA TTT
His Ile Met Gln Ala Gly Gln Thr Leu His Leu Gln Cys Arg Gly Glu Ala Ala His Lys>

      190      200      210      220      230      240
      *      *      *      *      *      *
TGG TCT TTG CCT GAA ATG GTG AGT AAG GAA AGC GAA AGG CTG AGC ATA ACT AAA TCT GCC
ACC AGA AAC GGA CTT TAC CAC TCA TTC CTT TCG CTT TCC GAC TCG TAT TGA TTT AGA CGG
Trp Ser Leu Pro Glu Met Val Ser Lys Glu Ser Glu Arg Leu Ser Ile Thr Lys Ser Ala>

      250      260      270      280      290      300
      *      *      *      *      *      *
TGT GGA AGA AAT GGC AAA CAA TTC TGC AGT ACT TTA ACC TTG AAC ACA GCT CAA GCA AAC
ACA CCT TCT TTA CCG TTT GTT AAG ACG TCA TGA AAT TGG AAC TTG TGT CGA GTT CGT TTG
Cys Gly Arg Asn Gly Lys Gln Phe Cys Ser Thr Leu Thr Leu Asn Thr Ala Gln Ala Asn>

      310      320      330      340      350      360
      *      *      *      *      *      *
CAC ACT GGC TTC TAC AGC TGC AAA TAT CTA GCT GTA CCT ACT TCA AAG AAG AAG GAA ACA
GTG TGA CCG AAG ATG TCG ACG TTT ATA GAT CGA CAT GGA TGA AGT TTC TTC TTC CTT TGT
His Thr Gly Phe Tyr Ser Cys Lys Tyr Leu Ala Val Pro Thr Ser Lys Lys Lys Glu Thr>

      370      380      390      400      410      420
      *      *      *      *      *      *
GAA TCT GCA ATC TAT ATA TTT ATT AGT GAT ACA GGT AGA CCT TTC GTA GAG ATG TAC AGT
CTT AGA CGT TAG ATA TAT AAA TAA TCA CTA TGT CCA TCT GGA AAG CAT CTC TAC ATG TCA
Glu Ser Ala Ile Tyr Ile Phe Ile Ser Asp Thr Gly Arg Pro Phe Val Glu Met Tyr Ser>

      430      440      450      460      470      480
      *      *      *      *      *      *
GAA ATC CCC GAA ATT ATA CAC ATG ACT GAA GGA AGG GAG CTC GTC ATT CCC TGC CGG GTT
CTT TAG GGG CTT TAA TAT GTG TAC TGA CTT CCT TCC CTC GAG CAG TAA GGG ACG GCC CAA
Glu Ile Pro Glu Ile Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val>

      490      500      510      520      530      540
      *      *      *      *      *      *
ACG TCA CCT AAC ATC ACT GTT ACT TTA AAA AAG TTT CCA CTT GAC ACT TTG ATC CCT GAT
TGC AGT GGA TTG TAG TGA CAA TGA AAT TTT TTC AAA GGT GAA CTG TGA AAC TAG GGA CTA
Thr Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro Asp>

```

550					560					570					580					590					600				
GGA	AAA	CGC	ATA	ATC	TGG	GAC	AGT	AGA	AAG	GGC	TTC	ATC	ATA	TCA	AAT	GCA	ACG	TAC	AAA										
CCT	TTT	GCG	TAT	TAG	ACC	CTG	TCA	TCT	TTC	CCG	AAG	TAG	TAT	AGT	TTA	CGT	TGC	ATG	TTT										
Gly	Lys	Arg	Ile	Ile	Trp	Asp	Ser	Arg	Lys	Gly	Phe	Ile	Ile	Ser	Asn	Ala	Thr	Tyr	Lys>										
610					620					630					640					650					660				
GAA	ATA	GGG	CTT	CTG	ACC	TGT	GAA	GCA	ACA	GTC	AAT	GGG	CAT	TTG	TAT	AAG	ACA	AAC	TAT										
CTT	TAT	CCC	GAA	GAC	TGG	ACA	CTT	CGT	TGT	CAG	TTA	CCC	GTA	AAC	ATA	TTC	TGT	TTG	ATA										
Glu	Ile	Gly	Leu	Leu	Thr	Cys	Glu	Ala	Thr	Val	Asn	Gly	His	Leu	Tyr	Lys	Thr	Asn	Tyr>										
670					680					690					700					710					720				
CTC	ACA	CAT	CGA	CAA	ACC	AAT	ACA	ATC	ATA	GAT	GTC	CAA	ATA	AGC	ACA	CCA	CGC	CCA	GTC										
GAG	TGT	GTA	GCT	GTT	TGG	TTA	TGT	TAG	TAT	CTA	CAG	GTT	TAT	TCG	TGT	GGT	GCG	GGT	CAG										
Leu	Thr	His	Arg	Gln	Thr	Asn	Thr	Ile	Ile	Asp	Val	Gln	Ile	Ser	Thr	Pro	Arg	Pro	Val>										
730					740					750					760					770					780				
AAA	TTA	CTT	AGA	GGC	CAT	ACT	CTT	GTC	CTC	AAT	TGT	ACT	GCT	ACC	ACT	CCC	TTG	AAC	ACG										
TTT	AAT	GAA	TCT	CCG	GTA	TGA	GAA	CAG	GAG	TTA	ACA	TGA	CGA	TGG	TGA	GGG	AAC	TTG	TGC										
Lys	Leu	Leu	Arg	Gly	His	Thr	Leu	Val	Leu	Asn	Cys	Thr	Ala	Thr	Thr	Pro	Leu	Asn	Thr>										
790					800					810					820					830					840				
AGA	GTT	CAA	ATG	ACC	TGG	AGT	TAC	CCT	GAT	GAA	ATT	GAC	CAA	AGC	AAT	TCC	CAT	GCC	AAC										
TCT	CAA	GTT	TAC	TGG	ACC	TCA	ATG	GGA	CTA	CTT	TAA	CTG	GTT	TCG	TTA	AGG	GTA	CGG	TTG										
Arg	Val	Gln	Met	Thr	Trp	Ser	Tyr	Pro	Asp	Glu	Ile	Asp	Gln	Ser	Asn	Ser	His	Ala	Asn>										
850					860					870					880					890					900				
ATA	TTC	TAC	AGT	GTT	CTT	ACT	ATT	GAC	AAA	ATG	CAG	AAC	AAA	GAC	AAA	GGA	CTT	TAT	ACT										
TAT	AAG	ATG	TCA	CAA	GAA	TGA	TAA	CTG	TTT	TAC	GTC	TTG	TTT	CTG	TTT	CCT	GAA	ATA	TGA										
Ile	Phe	Tyr	Ser	Val	Leu	Thr	Ile	Asp	Lys	Met	Gln	Asn	Lys	Asp	Lys	Gly	Leu	Tyr	Thr>										
910					920					930					940					950					960				
TGT	CGT	GTA	AGG	AGT	GGA	CCA	TCA	TTC	AAA	TCT	GTT	AAC	ACC	TCA	GTG	CAT	ATA	TAT	GAT										
ACA	GCA	CAT	TCC	TCA	CCT	GGT	AGT	AAG	TTT	AGA	CAA	TTG	TGG	AGT	CAC	GTA	TAT	ATA	CTA										
Cys	Arg	Val	Arg	Ser	Gly	Pro	Ser	Phe	Lys	Ser	Val	Asn	Thr	Ser	Val	His	Ile	Tyr	Asp>										
970					980					990					1000					1010					1020				
AAA	GCA	GGC	CCG	GGC	GAG	CCC	AAA	TCT	TGT	GAC	AAA	ACT	CAC	ACA	TGC	CCA	CCG	TGC	CCA										
TTT	CGT	CCG	GGC	CCG	CTC	GGG	TTT	AGA	ACA	CTG	TTT	TGA	GTG	TGT	ACG	GGT	GGC	ACG	GGT										
Lys	Ala	Gly	Pro	Gly	Glu	Pro	Lys	Ser	Cys	Asp	Lys	Thr	His	Thr	Cys	Pro	Pro	Cys	Pro>										
1030					1040					1050					1060					1070					1080				
GCA	CCT	GAA	CTC	CTG	GGG	GGA	CCG	TCA	GTC	TTC																			

1090				1100				1110				1120				1130				1140			
*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
CTC	ATG	ATC	TCC	CGG	ACC	CCT	GAG	GTC	ACA	TGC	GTG	GTG	GTG	GAC	GTG	AGC	CAC	GAA	GAC				
GAG	TAC	TAG	AGG	GCC	TGG	GGA	CTC	CAG	TGT	ACG	CAC	CAC	CAC	CTG	CAC	TCG	GTG	CTT	CTG				
Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His	Glu	Asp>				
1150				1160				1170				1180				1190				1200			
*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
CCT	GAG	GTC	AAG	TTC	AAC	TGG	TAC	GTG	GAC	GGC	GTG	GAG	GTG	CAT	AAT	GCC	AAG	ACA	AAG				
GGA	CTC	CAG	TTC	AAG	TTG	ACC	ATG	CAC	CTG	CCG	CAC	CTC	CAC	GTA	TTA	CGG	TTC	TGT	TTC				
Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys>				
1210				1220				1230				1240				1250				1260			
*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
CCG	CGG	GAG	GAG	CAG	TAC	AAC	AGC	ACG	TAC	CGT	GTG	GTC	AGC	GTC	CTC	ACC	GTC	CTG	CAC				
GGC	GCC	CTC	CTC	GTC	ATG	TTG	TCG	TGC	ATG	GCA	CAC	CAG	TCG	CAG	GAG	TGG	CAG	GAC	GTG				
Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser	Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His>				
1270				1280				1290				1300				1310				1320			
*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
CAG	GAC	TGG	CTG	AAT	GGC	AAG	GAG	TAC	AAG	TGC	AAG	GTC	TCC	AAC	AAA	GCC	CTC	CCA	GCC				
GTC	CTG	ACC	GAC	TTA	CCG	TTC	CTC	ATG	TTC	ACG	TTC	CAG	AGG	TTG	TTT	CGG	GAG	GGT	CGG				
Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu	Pro	Ala>				
1330				1340				1350				1360				1370				1380			
*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
CCC	ATC	GAG	AAA	ACC	ATC	TCC	AAA	GCC	AAA	GGG	CAG	CCC	CGA	GAA	CCA	CAG	GTG	TAC	ACC				
GGG	TAG	CTC	TTT	TGG	TAG	AGG	TTT	CGG	TTT	CCC	GTC	GGG	GCT	CTT	GGT	GTC	CAC	ATG	TGG				
Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr>				
1390				1400				1410				1420				1430				1440			
*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
CTG	CCC	CCA	TCC	CGG	GAT	GAG	CTG	ACC	AAG	AAC	CAG	GTC	AGC	CTG	ACC	TGC	CTG	GTC	AAA				
GAC	GGG	GGT	AGG	GCC	CTA	CTC	GAC	TGG	TTC	TTG	GTC	CAG	TCG	GAC	TGG	ACG	GAC	CAG	TTT				
Leu	Pro	Pro	Ser	Arg	Asp	Glu	Leu	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu	Val	Lys>				
1450				1460				1470				1480				1490				1500			
*	*	*	*	*																			

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Figure 13D

	1630		1640		1650		1660		1670								
	*	*	*	*	*	*	*	*	*								
GCT	CTG	CAC	AAC	CAC	TAC	ACG	CAG	AAG	AGC	CTC	TCC	CTG	TCT	CCG	GGT	AAA	TGA
CGA	GAC	GTG	TTG	GTG	ATG	TGC	GTC	TTC	TCG	GAG	AGG	GAC	AGA	GGC	CCA	TTT	ACT
Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Pro	Gly	Lys	***>

FOR REFERENCE

Figure 14A

			10				20				30				40				50				60
	*		*		*		*		*		*		*		*		*		*		*		*
ATG	GTC	AGC	TAC	TGG	GAC	ACC	GGG	GTC	CTG	CTG	TGC	GCG	CTG	CTC	AGC	TGT	CTG	CTT	CTC				
TAC	CAG	TCG	ATG	ACC	CTG	TGG	CCC	CAG	GAC	GAC	ACG	CGC	GAC	GAG	TCG	ACA	GAC	GAA	GAG				
Met	Val	Ser	Tyr	Trp	Asp	Thr	Gly	Val	Leu	Leu	Cys	Ala	Leu	Leu	Ser	Cys	Leu	Leu	Leu				
			70				80				90				100				110				120
	*		*		*		*		*		*		*		*		*		*		*		*
ACA	GGA	TCT	AGT	TCC	GGA	GGT	AGA	CCT	TTC	GTA	GAG	ATG	TAC	AGT	GAA	ATC	CCC	GAA	ATT				
TGT	CCT	AGA	TCA	AGG	CCT	CCA	TCT	GGA	AAG	CAT	CTC	TAC	ATG	TCA	CTT	TAG	GGG	CTT	TAA				
Thr	Gly	Ser	Ser	Ser	Gly	Gly	Arg	Pro	Phe	Val	Glu	Met	Tyr	Ser	Glu	Ile	Pro	Glu	Ile				
			130				140				150				160				170				180
	*		*		*		*		*		*		*		*		*		*		*		*
ATA	CAC	ATG	ACT	GAA	GGA	AGG	GAG	CTC	GTC	ATT	CCC	TGC	CGG	GTT	ACG	TCA	CCT	AAC	ATC				
TAT	GTG	TAC	TGA	CTT	CCT	TCC	CTC	GAG	CAG	TAA	GGG	ACG	GCC	CAA	TGC	AGT	GGA	TTG	TAG				
Ile	His	Met	Thr	Glu	Gly	Arg	Glu	Leu	Val	Ile	Pro	Cys	Arg	Val	Thr	Ser	Pro	Asn	Ile				
			190				200				210				220				230				240
	*		*		*		*		*		*		*		*		*		*		*		*
ACT	GTT	ACT	TTA	AAA	AAG	TTT	CCA	CTT	GAC	ACT	TTG	ATC	CCT	GAT	GGA	AAA	CGC	ATA	ATC				
TGA	CAA	TGA	AAT	TTT	TTC	AAA	GGT	GAA	CTG	TGA	AAC	TAG	GGA	CTA	CCT	TTT	GCG	TAT	TAG				
Thr	Val	Thr	Leu	Lys	Lys	Phe	Pro	Leu	Asp	Thr	Leu	Ile	Pro	Asp	Gly	Lys	Arg	Ile	Ile				
			250				260				270				280				290				300
	*		*		*		*		*		*		*		*		*		*		*		*
TGG	GAC	AGT	AGA	AAG	GGC	TTC	ATC	ATA	TCA	AAT	GCA	ACG	TAC	AAA	GAA	ATA	GGG	CTT	CTG				
ACC	CTG	TCA	TCT	TTC	CCG	AAG	TAG	TAT	AGT	TTA	CGT	TGC	ATG	TTT	CTT	TAT	CCC	GAA	GAC				
Trp	Asp	Ser	Arg	Lys	Gly	Phe	Ile	Ile	Ser	Asn	Ala	Thr	Tyr	Lys	Glu	Ile	Gly	Leu	Leu				
			310				320				330				340				350				360
	*		*		*		*		*		*		*		*		*		*		*		*
ACC	TGT	GAA	GCA	ACA	GTC	AAT	GGG	CAT	TTG	TAT	AAG	ACA	AAC	TAT	CTC	ACA	CAT	CGA	CAA				
TGG	ACA	CTT	CGT	TGT	CAG	TTA	CCC	GTA	AAC	ATA	TTC	TGT	TTG	ATA	GAG	TGT	GTA	GCT	GTT				
Thr	Cys	Glu	Ala	Thr	Val	Asn	Gly	His	Leu	Tyr	Lys	Thr	Asn	Tyr	Leu	Thr	His	Arg	Gln				
			370				380				390				400				410				420
	*		*		*		*		*		*		*		*		*		*		*		*
ACC	AAT	ACA	ATC	ATA	GAT	GTC	CAA	ATA	AGC	ACA	CCA	CGC	CCA	GTC	AAA	TTA	CTT	AGA	GGC				
TGG	TTA	TGT	TAG	TAT	CTA	CAG	GTT	TAT	TCG	TGT	GGT	GCG	GGT	CAG	TTT	AAT	GAA	TCT	CCG				
Thr	Asn	Thr	Ile	Ile	Asp	Val	Gln	Ile	Ser	Thr	Pro	Arg	Pro	Val	Lys	Leu	Leu	Arg	Gly				
			430				440				450				460				470				480
	*		*		*		*		*		*		*		*		*		*		*		*
CAT	ACT	CTT	GTC	CTC	AAT	TGT	ACT	GCT	ACC	ACT	CCC	TTG	AAC	ACG	AGA	GTT	CAA	ATG	ACC				
GTA	TGA	GAA	CAG	GAG	TTA	ACA	TGA	CGA	TGG	TGA	GGG	AAC	TTG	TGC	TCT	CAA	GTT	TAC	TGG				
His	Thr	Leu	Val	Leu	Asn	Cys	Thr	Ala	Thr	Thr	Pro	Leu	Asn	Thr	Arg	Val	Gln	Met	Thr				
			490				500				510				520				530				540
	*		*		*		*		*		*		*		*		*		*		*		*
TGG	AGT	TAC	CCT	GAT	GAA	ATT	GAC	CAA	AGC	AAT	TCC	CAT	GCC	AAC	ATA	TTC	TAC	AGT	GTT				
ACC	TCA	ATG	GGA	CTA	CTT	TAA	CTG	GTT	TCG	TTA	AGG	GTA	CGG	TTG	TAT	AAG	ATG	TCA	CAA				
Trp	Ser	Tyr	Pro	Asp	Glu	Ile	Asp	Gln	Ser	Asn	Ser	His	Ala	Asn	Ile	Phe	Tyr	Ser	Val				

T.D.T.F.D. 22.06.19

Figure 14C

1090	1100	1110	1120	1130	1140
* * *	* *	* *	* *	* *	* *
GAT GAG CTG ACC AAG AAC CAG GTC AGC CTG ACC TGC CTG GTC AAA GGC TTC TAT CCC AGC					
CTA CTC GAC TGG TTC TTG GTC CAG TCG GAC TGG ACG GAC CAG TTT CCG AAG ATA GGG TCG					
Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser>					
1150	1160	1170	1180	1190	1200
* * *	* *	* *	* *	* *	* *
GAC ATC GCC GTG GAG TGG GAG AGC AAT GGG CAG CCG GAG AAC AAC TAC AAG ACC ACG CCT					
CTG TAG CCG CAC CTC ACC CTC TCG TTA CCC GTC GGC CTC TTG TTG ATG TTC TGG TGC GGA					
Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro>					
1210	1220	1230	1240	1250	1260
* * *	* *	* *	* *	* *	* *
CCC GTG CTG GAC TCC GAC GGC TCC TTC TTC CTC TAC AGC AAG CTC ACC GTG GAC AAG AGC					
GGG CAC GAC CTG AGG CTG CCG AGG AAG AAG GAG ATG TCG TTC GAG TGG CAC CTG TTC TCG					
Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser>					
1270	1280	1290	1300	1310	1320
* * *	* *	* *	* *	* *	* *
AGG TGG CAG CAG GGG AAC GTC TTC TCA TGC TCC GTG ATG CAT GAG GCT CTG CAC AAC CAC					
TCC ACC GTC GTC CCC TTG CAG AAG AGT ACG AGG CAC TAC GTA CTC CGA GAC GTG TTG GTG					
Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His>					
1330	1340	1350			
* * *	* *	* *			
TAC ACG CAG AAG AGC CTC TCC CTG TCT CCG GGT AAA TGA					
ATG TGC GTC TTC TCG GAG AGG GAC AGA GGC CCA TTT ACT					
Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys ***>					

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Figure 15A

10 20 30 40 50 60
 * * * * *
 ATG GTC AGC TAC TGG GAC ACC GGG GTC CTG CTG TGC GCG CTG CTC AGC TGT CTG CTT CTC
 TAC CAG TCG ATG ACC CTG TGG CCC CAG GAC GAC ACG CGC GAC GAG TCG ACA GAC GAA GAG
 Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser Cys Leu Leu Leu>

70 80 90 100 110 120
 * * * * *
 ACA GGA TCT AGT TCC GGA GGT AGA CCT TTC GTA GAG ATG TAC AGT GAA ATC CCC GAA ATT
 TGT CCT AGA TCA AGG CCT CCA TCT GGA AAG CAT CTC TAC ATG TCA CTT TAG GGG CTT TAA
 Thr Gly Ser Ser Ser Gly Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu Ile>

130 140 150 160 170 180
 * * * * *
 ATA CAC ATG ACT GAA GGA AGG GAG CTC GTC ATT CCC TGC CGG GTT ACG TCA CCT AAC ATC
 TAT GTG TAC TGA CTT CCT TCC CTC GAG CAG TAA GGG ACG GCC CAA TGC AGT GGA TTG TAG
 Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val Thr Ser Pro Asn Ile>

190 200 210 220 230 240
 * * * * *
 ACT GTT ACT TTA AAA AAG TTT CCA CTT GAC ACT TTG ATC CCT GAT GGA AAA CGC ATA ATC
 TGA CAA TGA AAT TTT TTC AAA GGT GAA CTG TGA AAC TAG GGA CTA CCT TTT GCG TAT TAG
 Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro Asp Gly Lys Arg Ile Ile>

250 260 270 280 290 300
 * * * * *
 TGG GAC AGT AGA AAG GGC TTC ATC ATA TCA AAT GCA ACG TAC AAA GAA ATA GGG CTT CTG
 ACC CTG TCA TCT TTC CCG AAG TAG TAT AGT TTA CGT TGC ATG TTT CTT TAT CCC GAA GAC
 Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu>

310 320 330 340 350 360
 * * * * *
 ACC TGT GAA GCA ACA GTC AAT GGG CAT TTG TAT AAG ACA AAC TAT CTC ACA CAT CGA CAA
 TGG ACA CTT CGT TGT CAG TTA CCC GTA AAC ATA TTC TGT TTG ATA GAG TGT GTA GCT GTT
 Thr Cys Glu Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg Gln>

370 380 390 400 410 420
 * * * * *
 ACC AAT ACA ATC ATA GAT GTC CAA ATA AGC ACA CCA CGC CCA GTC AAA TTA CTT AGA GGC
 TGG TTA TGT TAG TAT CTA CAG GTT TAT TCG TGT GGT GCG GGT CAG TTT AAT GAA TCT CCG
 Thr Asn Thr Ile Ile Asp Val Gln Ile Ser Thr Pro Arg Pro Val Lys Leu Leu Arg Gly>

430 440 450 460 470 480
 * * * * *
 CAT ACT CTT GTC CTC AAT TGT ACT GCT ACC ACT CCC TTG AAC ACG AGA GTT CAA ATG ACC
 GTA TGA GAA CAG GAG TTA ACA TGA CGA TGG TGA GGG AAC TTG TGC TCT CAA GTT TAC TGG
 His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr Pro Leu Asn Thr Arg Val Gln Met Thr>

490 500 510 520 530 540
 * * * * *
 TGG AGT TAC CCT GAT GAA AAA AAT AAG AGA GCT TCC GTA AGG CGA CGA ATT GAC CAA AGC
 ACC TCA ATG GGA CTA CTT TTT TTA TTC TCT CGA AGG CAT TCC GCT GCT TAA CTG GTT TCG
 Trp Ser Tyr Pro Asp Glu Lys Asn Lys Arg Ala Ser Val Arg Arg Arg Ile Asp Gln Ser>

2232260
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Figure 15C

1090				1100				1110				1120				1130				1140			
*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*		
CCA	CAG	GTG	TAC	ACC	CTG	CCC	CCA	TCC	CGG	GAT	GAG	CTG	ACC	AAG	AAC	CAG	GTC	AGC	CTG				
GGT	GTC	CAC	ATG	TGG	GAC	GGG	GGT	AGG	GCC	CTA	CTC	GAC	TGG	TTC	TTG	GTC	CAG	TCG	GAC				
Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Arg	Asp	Glu	Leu	Thr	Lys	Asn	Gln	Val	Ser	Leu>				
1150				1160				1170				1180				1190				1200			
*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*		
ACC	TGC	CTG	GTC	AAA	GGC	TTC	TAT	CCC	AGC	GAC	ATC	GCC	GTG	GAG	TGG	GAG	AGC	AAT	GGG				
TGG	ACG	GAC	CAG	TTT	CCG	AAG	ATA	GGG	TCG	CTG	TAG	CGG	CAC	CTC	ACC	CTC	TCG	TTA	CCC				
Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly>				
1210				1220				1230				1240				1250				1260			
*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*		
CAG	CCG	GAG	AAC	AAC	TAC	AAG	ACC	ACG	CCT	CCC	GTG	CTG	GAC	TCC	GAC	GGC	TCC	TTC	TTC				
GTC	GGC	CTC	TTG	TTG	ATG	TTC	TGG	TGC	GGA	GGG	CAC	GAC	CTG	AGG	CTG	CCG	AGG	AAG	AAG				
Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe>				
1270				1280				1290				1300				1310				1320			
*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*		
CTC	TAC	AGC	AAG	CTC	ACC	GTG	GAC	AAG	AGC	AGG	TGG	CAG	CAG	GGG	AAC	GTC	TTC	TCA	TGC				
GAG	ATG	TCG	TTC	GAG	TGG	CAC	CTG	TTC	TCG	TCC	ACC	GTC	GTC	CCC	TTG	CAG	AAG	AGT	ACG				
Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys>				
1330				1340				1350				1360				1370				1380			
*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*		
TCC	GTG	ATG	CAT	GAG	GCT	CTG	CAC	AAC	CAC	TAC	ACG	CAG	AAG	AGC	CTC	TCC	CTG	TCT	CCG				
AGG	CAC	TAC	GTA	CTC	CGA	GAC	GTG	TTG	GTG	ATG	TGC	GTC	TTC	TCG	GAG	AGG	GAC	AGA	GGC				
Ser	Val	Met	His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Pro>				
* GGT AAA TGA CCA TTT ACT Gly Lys ***>																							

Figure 16A

```

      10      20      30      40      50      60
      *      *      *      *      *      *
ATG GTC AGC TAC TGG GAC ACC GGG GTC CTG CTG TGC GCG CTG CTC AGC TGT CTG CTT CTC
TAC CAG TCG ATG ACC CTG TGG CCC CAG GAC GAC ACG CGC GAC GAG TCG ACA GAC GAA GAG
Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser Cys Leu Leu Leu>

      70      80      90      100      110      120
      *      *      *      *      *      *
ACA GGA TCT AGT TCA GGT TCA AAA TTA AAA GAT CCT GAA CTG AGT TTA AAA GGC ACC CAG
TGT CCT AGA TCA AGT CCA AGT TTT AAT TTT CTA GGA CTT GAC TCA AAT TTT CCG TGG GTC
Thr Gly Ser Ser Ser Gly Ser Lys Leu Lys Asp Pro Glu Leu Ser Leu Lys Gly Thr Gln>

      130      140      150      160      170      180
      *      *      *      *      *      *
CAC ATC ATG CAA GCA GGC CAG ACA CTG CAT CTC CAA TGC AGG GGG GAA GCA GCC CAT AAA
GTG TAG TAC GTT CGT CCG GTC TGT GAC GTA GAG GTT ACG TCC CCC CTT CGT CGG GTA TTT
His Ile Met Gln Ala Gly Gln Thr Leu His Leu Gln Cys Arg Gly Glu Ala Ala His Lys>

      190      200      210      220      230      240
      *      *      *      *      *      *
TGG TCT TTG CCT GAA ATG GTG AGT AAG GAA AGC GAA AGG CTG AGC ATA ACT AAA TCT GCC
ACC AGA AAC GGA CTT TAC CAC TCA TTC CTT TCG CTT TCC GAC TCG TAT TGA TTT AGA CGG
Trp Ser Leu Pro Glu Met Val Ser Lys Glu Ser Glu Arg Leu Ser Ile Thr Lys Ser Ala>

      250      260      270      280      290      300
      *      *      *      *      *      *
TGT GGA AGA AAT GGC AAA CAA TTC TGC AGT ACT TTA ACC TTG AAC ACA GCT CAA GCA AAC
ACA CCT TCT TTA CCG TTT GTT AAG ACG TCA TGA AAT TGG AAC TTG TGT CGA GTT CGT TTG
Cys Gly Arg Asn Gly Lys Gln Phe Cys Ser Thr Leu Thr Leu Asn Thr Ala Gln Ala Asn>

      310      320      330      340      350      360
      *      *      *      *      *      *
CAC ACT GGC TTC TAC AGC TGC AAA TAT CTA GCT GTA CCT ACT TCA AAG AAG AAG GAA ACA
GTG TGA CCG AAG ATG TCG ACG TTT ATA GAT CGA CAT GGA TGA AGT TTC TTC TTC CTT TGT
His Thr Gly Phe Tyr Ser Cys Lys Tyr Leu Ala Val Pro Thr Ser Lys Lys Lys Glu Thr>

      370      380      390      400      410      420
      *      *      *      *      *      *
GAA TCT GCA ATC TAT ATA TTT ATT AGT GAT ACA GGT AGA CCT TTC GTA GAG ATG TAC AGT
CTT AGA CGT TAG ATA TAT AAA TAA TCA CTA TGT CCA TCT GGA AAG CAT CTC TAC ATG TCA
Glu Ser Ala Ile Tyr Ile Phe Ile Ser Asp Thr Gly Arg Pro Phe Val Glu Met Tyr Ser>

      430      440      450      460      470      480
      *      *      *      *      *      *
GAA ATC CCC GAA ATT ATA CAC ATG ACT GAA GGA AGG GAG CTC GTC ATT CCC TGC CGG GTT
CTT TAG GGG CTT TAA TAT GTG TAC TGA CTT CCT TCC CTC GAG CAG TAA GGG ACG GCC CAA
Glu Ile Pro Glu Ile Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val>

      490      500      510      520      530      540
      *      *      *      *      *      *
ACG TCA CCT AAC ATC ACT GTT ACT TTA AAA AAG TTT CCA CTT GAC ACT TTG ATC CCT GAT
TGC AGT GGA TTG TAG TGA CAA TGA AAT TTT TTC AAA GGT GAA CTG TGA AAC TAG GGA CTA
Thr Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro Asp>

```

T01E043E260

550				560				570				580				590				600			
*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
GGA	AAA	CGC	ATA	ATC	TGG	GAC	AGT	AGA	AAG	GGC	TTC	ATC	ATA	TCA	AAT	GCA	ACG	TAC	AAA				
CCT	TTT	GCG	TAT	TAG	ACC	CTG	TCA	TCT	TTC	CCG	AAG	TAG	TAT	AGT	TTA	CGT	TGC	ATG	TTT				
Gly	Lys	Arg	Ile	Ile	Trp	Asp	Ser	Arg	Lys	Gly	Phe	Ile	Ile	Ser	Asn	Ala	Thr	Tyr	Lys	>			
610				620				630				640				650				660			
*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
GAA	ATA	GGG	CTT	CTG	ACC	TGT	GAA	GCA	ACA	GTC	AAT	GGG	CAT	TTG	TAT	AAG	ACA	AAC	TAT				
CTT	TAT	CCC	GAA	GAC	TGG	ACA	CTT	CGT	TGT	CAG	TTA	CCC	GTA	AAC	ATA	TTC	TGT	TTG	ATA				
Glu	Ile	Gly	Leu	Leu	Thr	Cys	Glu	Ala	Thr	Val	Asn	Gly	His	Leu	Tyr	Lys	Thr	Asn	Tyr	>			
670				680				690				700				710				720			
*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
CTC	ACA	CAT	CGA	CAA	ACC	AAT	ACA	ATC	ATA	GAT	GTC	CAA	ATA	AGC	ACA	CCA	CGC	CCA	GTC				
GAG	TGT	GTA	GCT	GTT	TGG	TTA	TGT	TAG	TAT	CTA	CAG	GTT	TAT	TCG	TGT	GGT	GCG	GGT	CAG				
Leu	Thr	His	Arg	Gln	Thr	Asn	Thr	Ile	Ile	Asp	Val	Gln	Ile	Ser	Thr	Pro	Arg	Pro	Val	>			
730				740				750				760				770				780			
*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
AAA	TTA	CTT	AGA	GGC	CAT	ACT	CTT	GTC	CTC	AAT	TGT	ACT	GCT	ACC	ACT	CCC	TTG	AAC	ACG				
TTT	AAT	GAA	TCT	CCG	GTA	TGA	GAA	CAG	GAG	TTA	ACA	TGA	CGA	TGG	TGA	GGG	AAC	TTG	TGC				
Lys	Leu	Leu	Arg	Gly	His	Thr	Leu	Val	Leu	Asn	Cys	Thr	Ala	Thr	Thr	Pro	Leu	Asn	Thr	>			
790				800				810				820				830				840			
*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
AGA	GTT	CAA	ATG	ACC	TGG	AGT	TAC	CCT	GAT	GAA	AAA	AAT	AAG	AAC	GCT	TCC	GTA	AGG	CGA				
TCT	CAA	GTT	TAC	TGG	ACC	TCA	ATG	GGA	CTA	CTT	TTT	TTA	TTC	TTG	CGA	AGG	CAT	TCC	GCT				
Arg	Val	Gln	Met	Thr	Trp	Ser	Tyr	Pro	Asp	Glu	Lys	Asn	Lys	Asn	Ala	Ser	Val	Arg	Arg	>			
850				860				870				880				890				900			
*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
CGA	ATT	GAC	CAA	AGC	AAT	TCC	CAT	GCC	AAC	ATA	TTC	TAC	AGT	GTT	CTT	ACT	ATT	GAC	AAA				
GCT	TAA	CTG	GTT	TCG	TTA	AGG	GTA	CGG	TTG	TAT	AAG	ATG	TCA	CAA	GAA	TGA	TAA	CTG	TTT				
Arg	Ile	Asp	Gln	Ser	Asn	Ser	His	Ala	Asn	Ile	Phe	Tyr	Ser	Val	Leu	Thr	Ile	Asp	Lys	>			
910				920				930				940				950				960			
*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
ATG	CAG	AAC	AAA	GAC	AAA	GGA	CTT	TAT	ACT	TGT	CGT	GTA	AGG	AGT	GGA	CCA	TCA	TTC	AAA				

Figure 16C

1090	1100	1110	1120	1130	1140
* * *	* * *	* * *	* * *	* * *	* * *
TTC CTC TTC CCC CCA AAA CCC AAG GAC ACC CTC ATG ATC TCC CGG ACC CCT GAG GTC ACA	AAG GAG AAG GGG GGT TTT GGG TTC CTG TGG GAG TAC TAG AGG GCC TGG GGA CTC CAG TGT	Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr>			
1150	1160	1170	1180	1190	1200
* * *	* * *	* * *	* * *	* * *	* * *
TGC GTG GTG GTG GAC GTG AGC CAC GAA GAC CCT GAG GTC AAG TTC AAC TGG TAC GTG GAC	ACG CAC CAC CAC CTG CAC TCG GTG CTT CTG GGA CTC CAG TTC AAG TTG ACC ATG CAC CTG	Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp>			
1210	1220	1230	1240	1250	1260
* * *	* * *	* * *	* * *	* * *	* * *
GGC GTG GAG GTG CAT AAT GCC AAG ACA AAG CCG CGG GAG GAG CAG TAC AAC AGC ACG TAC	CCG CAC CTC CAC GTA TTA CGG TTC TGT TTC GGC GCC CTC CTC GTC ATG TTG TCG TGC ATG	Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr>			
1270	1280	1290	1300	1310	1320
* * *	* * *	* * *	* * *	* * *	* * *
CGT GTG GTC AGC GTC CTC ACC GTC CTG CAC CAG GAC TGG CTG AAT GGC AAG GAG TAC AAG	GCA CAC CAG TCG CAG GAG TGG CAG GAC GTG GTC CTG ACC GAC TTA CCG TTC CTC ATG TTC	Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys>			
1330	1340	1350	1360	1370	1380
* * *	* * *	* * *	* * *	* * *	* * *
TGC AAG GTC TCC AAC AAA GCC CTC CCA GCC CCC ATC GAG AAA ACC ATC TCC AAA GCC AAA	ACG TTC CAG AGG TTG TTT CGG GAG GGT CGG GGG TAG CTC TTT TGG TAG AGG TTT CGG TTT	Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys>			
1390	1400	1410	1420	1430	1440
* * *	* * *	* * *	* * *	* * *	* * *
GGG CAG CCC CGA GAA CCA CAG GTG TAC ACC CTG CCC CCA TCC CGG GAT GAG CTG ACC AAG	CCC GTC GGG GCT CTT GGT GTC CAC ATG TGG GAC GGG GGT AGG GCC CTA CTC GAC TGG TTC	Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys>			
1450	1460	1470	1480	1490	1500
* * *	* * *	* * *	* * *	* * *	* * *
AAC CAG GTC AGC CTG ACC TGC CTG GTC AAA GGC TTC TAT CCC AGC GAC ATC GCC GTG GAG	TTG GTC CAG TCG GAC TGG ACG GAC CAG TTT CCG AAG ATA GGG TCG CTG TAG CGG CAC CTC	Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu>			
1510	1520	1530	1540	1550	1560
* * *	* * *	* * *	* * *	* * *	* * *
TGG GAG AGC AAT GGG CAG CCG GAG AAC AAC TAC AAG ACC ACG CCT CCC GTG CTG GAC TCC	ACC CTC TCG TTA CCC GTC GGC CTC TTG TTG ATG TTC TGG TGC GGA GGG CAC GAC CTG AGG	Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser>			
1570	1580	1590	1600	1610	1620
* * *	* * *	* * *	* * *	* * *	* * *
GAC GGC TCC TTC TTC CTC TAC AGC AAG CTC ACC GTG GAC AAG AGC AGG TGG CAG CAG GGG	CTG CCG AGG AAG AAG GAG ATG TCG TTC GAG TGG CAC CTG TTC TCG TCC ACC GTC GTC CCC	Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly>			

Figure 16D

[illegible]

Figure 17

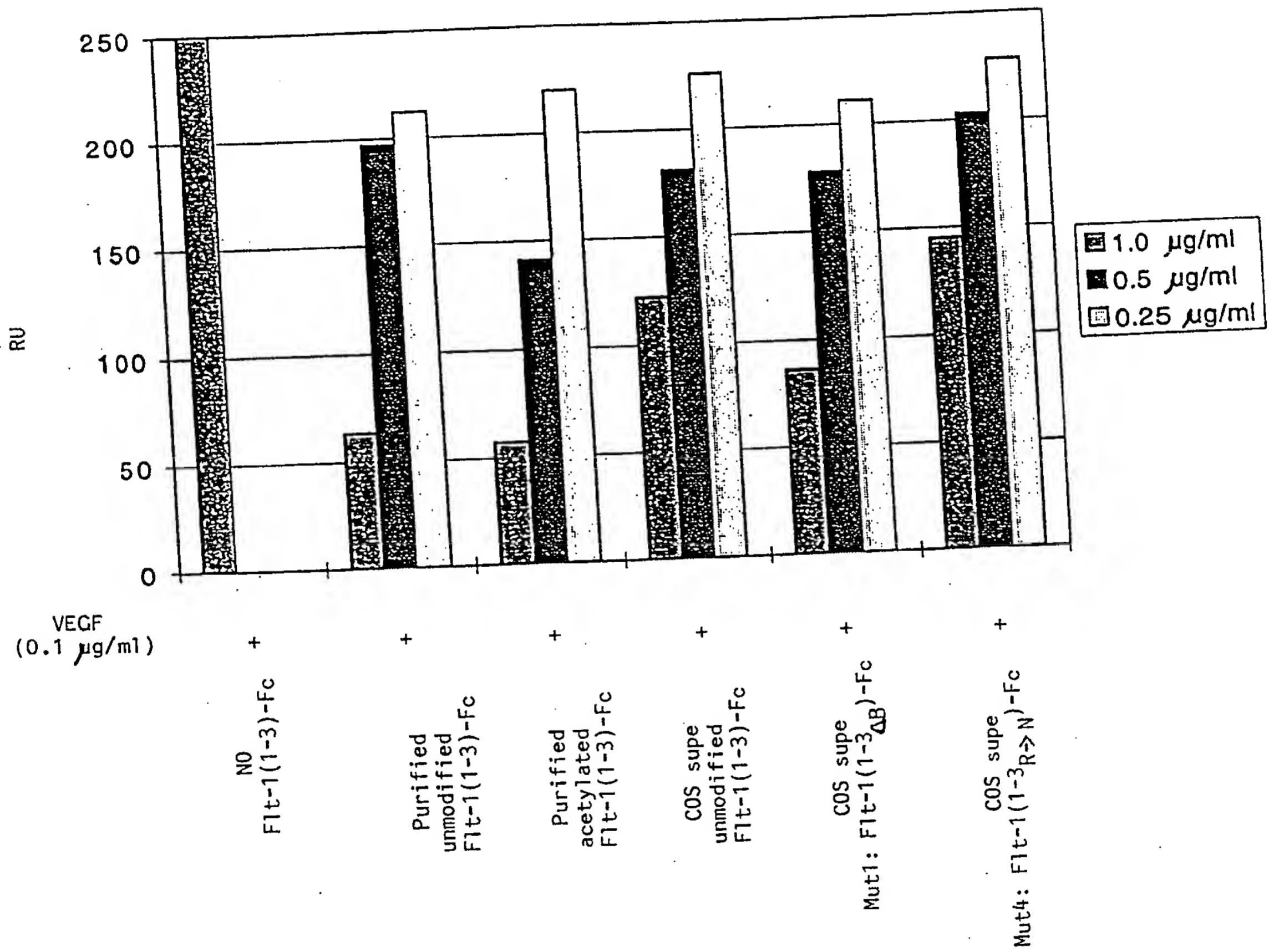


Figure 18

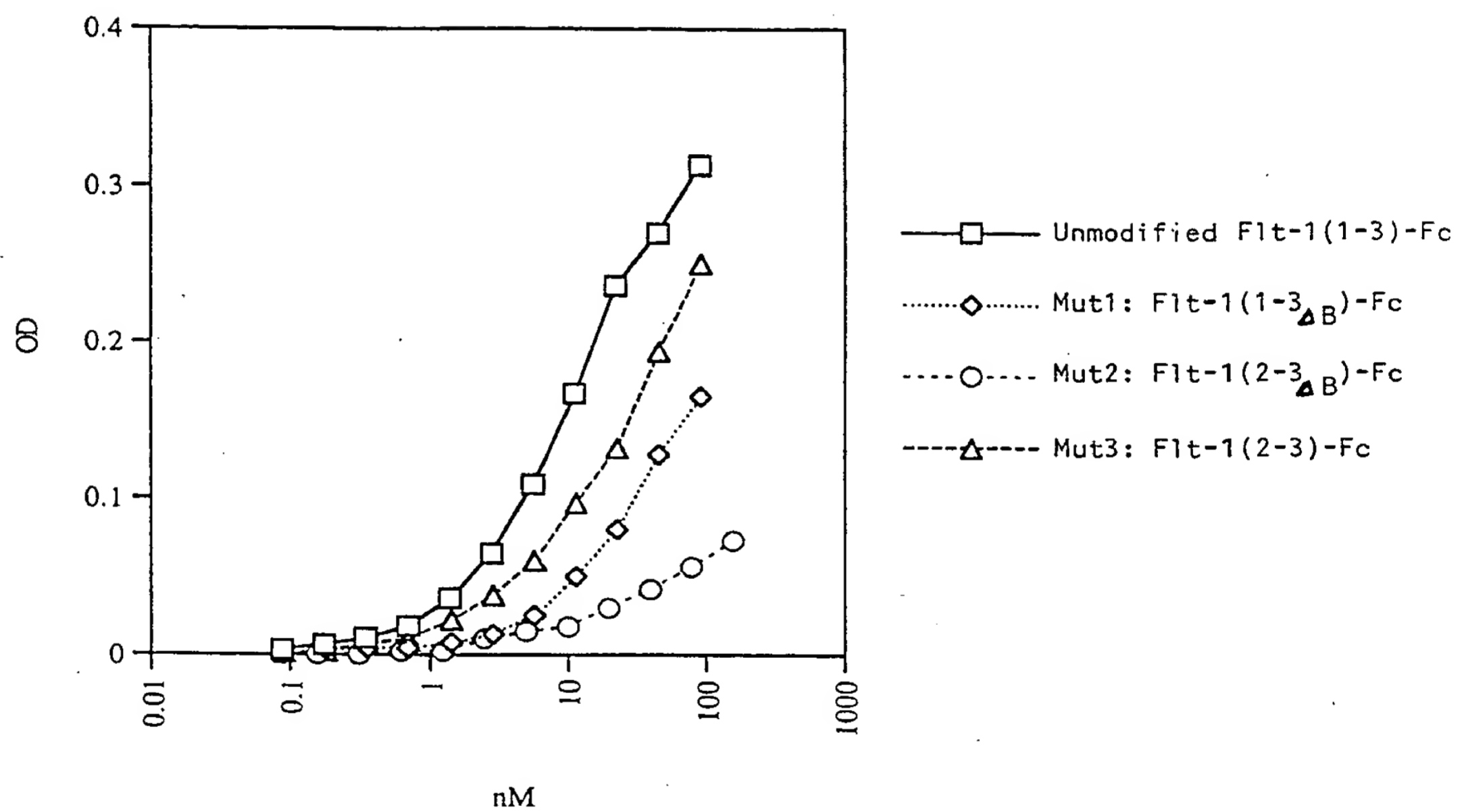


Figure 19

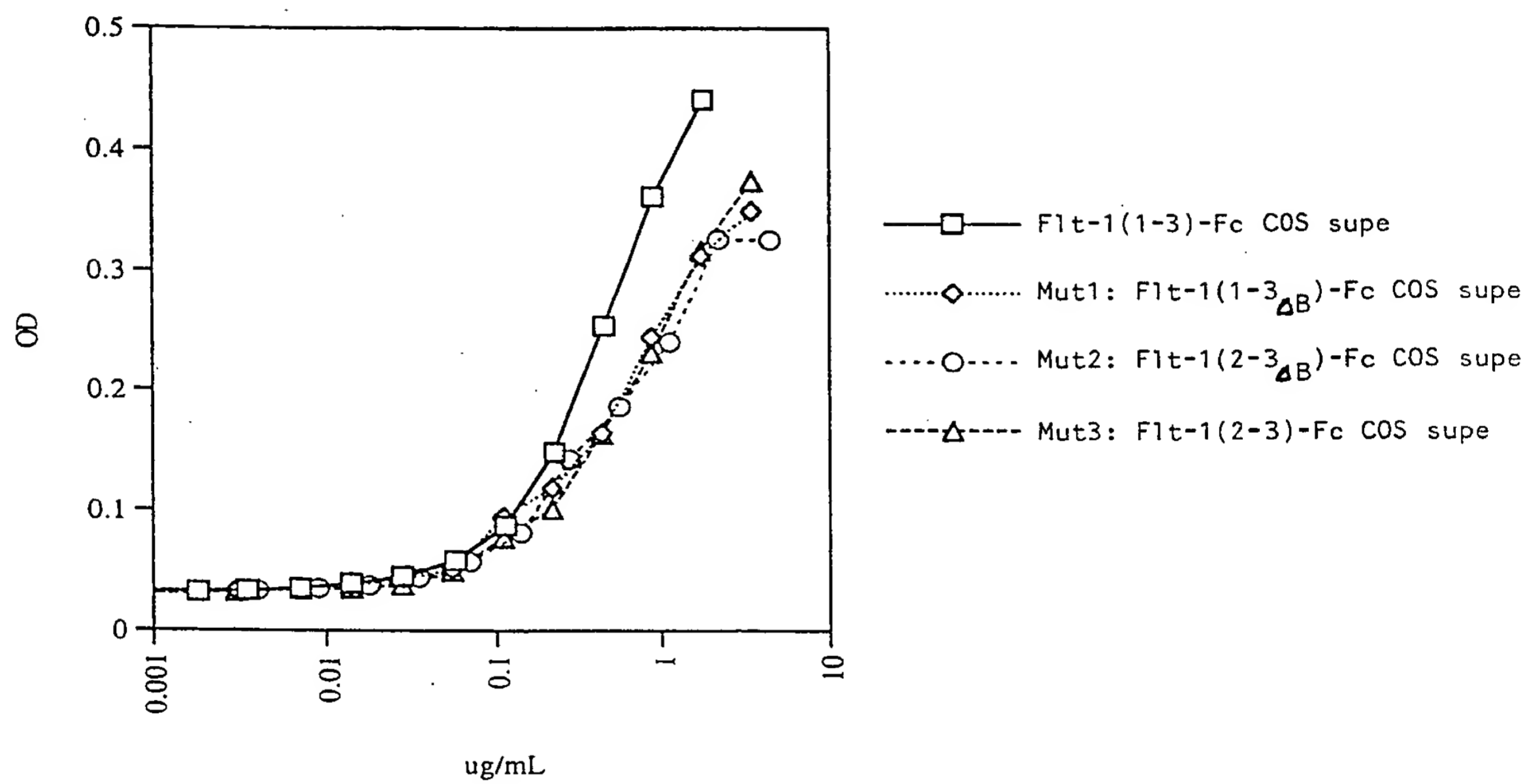


Figure 20

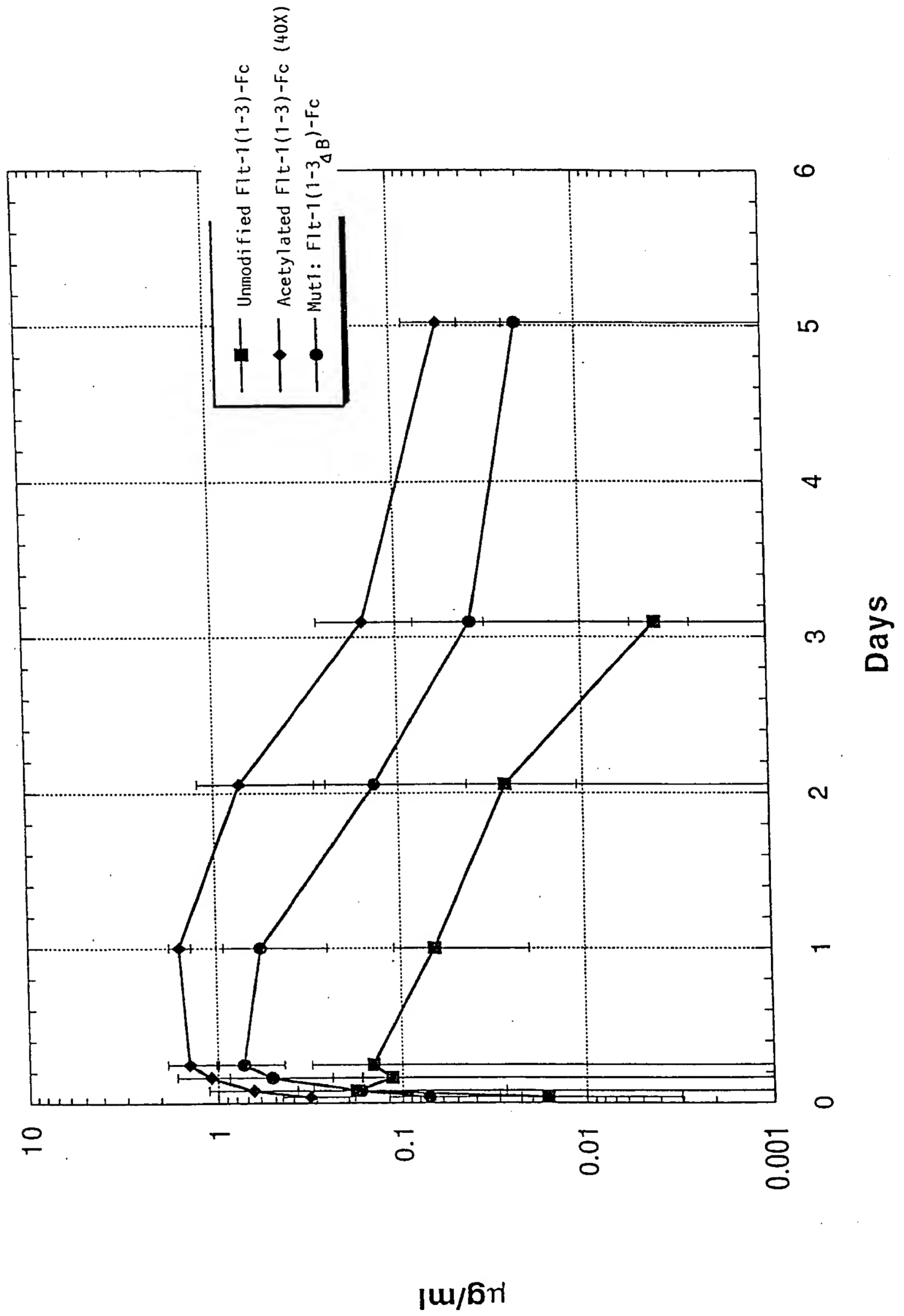


Figure 21A

```

                                >EcoRI_site
                                |
    10      20      30      40      50      60      70      80
AAGCTTGGGCTGCAGGTCGATCGACTCTAGAGGATCGATCCCCGGGCGAGCTCGAATTCGCAACCACCATGGTTCAGCTAC
TTCGAACCCGACGTCCAGCTAGCTGAGATCTCCTAGCTAGGGGCCCGCTCGAGCTTAAGCGTTGGTGGTACCAGTCGATG
                                M V S Y>
                                1      4
                                _____>

                                >BspEI_bridge
                                |
    90      100     110     120     130     140     150     160
TGGGACACCGGGGTCCTGCTGTGCGCGCTGCTCAGCTGTCTGCTTCTCACAGGATCTAGTTCCGGAGGTAGACCTTTTCGT
ACCCTGTGGCCCCAGGACGACACGCGCGACGAGTCGACAGACGAAGAGTGTCTAGATCAAGGCCTCCATCTGGAAAGCA
W D T G V L L C A L L S C L L L T G S S>
                                _____>
                                FLT1 SS
                                _____>
                                S G>
                                _____>
                                G R P F V>
                                _____>
                                31

    170     180     190     200     210     220     230     240
AGAGATGTACAGTGAAATCCCCGAAATTATACACATGACTGAAGGAAGGGAGCTCGTCATTCCCTGCCGGGTTACGTCAC
TCTCTACATGTCACCTTTAGGGGCTTTAATATGTGTACTGACTTCCTTCCCTCGAGCAGTAAGGGACGGCCCAATGCAGTG
E M Y S E I P E I I H M T E G R E L V I P C R V T S>
                                _____>
                                57
                                _____>
                                HFLT1 D2
                                _____>

    250     260     270     280     290     300     310     320
CTAACATCACTGTTACTTTAAAAAAGTTTCCACTTGACACTTTGATCCCTGATGGAAAACGCATAATCTGGGACAGTAGA
GATTGTAGTGACAATGAAATTTTTTCAAAGGTGAACTGTGAAACTAGGGACTACCTTTTGCGTATTAGACCCTGTCATCT
P N I T V T L K K F P L D T L I P D G K R I I W D S R>
                                _____>
                                84
                                _____>
                                HFLT1 D2
                                _____>

    330     340     350     360     370     380     390     400
AAGGGCTTCATCATATCAAATGCAACGTACAAAGAAATAGGGCTTCTGACCTGTGAAGCAACAGTCAATGGGCATTTGTA
TTCCCGAAGTAGTATAGTTTACGTTGCATGTTTCTTTATCCCGAAGACTGGACACTTCGTTGTGAGTTACCCGTAAACAT
K G F I I S N A T Y K E I G L L T C E A T V N G H L Y>
                                _____>
                                111
                                _____>
                                HFLT1 D2
                                _____>

    410     420     430     440     450     460     470     480
TAAGACAAACTATCTCACACATCGACAAACCAATACAATCATAGATGTGGTTCTGAGTCCGTCTCATGGAATTGAACTAT
ATTCTGTTTGATAGAGTGTGTAGCTGTTTGGTTATGTTAGTATCTACACCAAGACTCAGGCAGAGTACCTTAACCTTGATA
K T N Y L T H R Q T N T I I D>
                                _____>
                                HFLT1 D2
                                _____>
                                V V L S P S H G I E L>
                                _____>
                                137
                                _____>
                                HFLK1 D3
                                _____>

```

Figure 21B

```

      490      500      510      520      530      540      550      560
CTGTTGGAGAAAAGCTTGTCTTAAATTTGTACAGCAAGAACTGAACTAAATGTGGGGATTGACTTCAACTGGGAATACCCCT
GACAACCTCTTTTTCGAACAGAATTTAACATGTCGTTCTTGACTTGATTTACACCCCTAACTGAAGTTGACCCCTATGGGA
S V G E K L V L N C T A R T E L N V G I D F N W E Y P>
                                                                164
_____HFLK1 D3_____>

      570      580      590      600      610      620      630      640
TCTTCGAAGCATCAGCATAAGAACTTTGTAAACCGAGACCTAAAAACCCAGTCTGGGAGTGAGATGAAGAAATTTTGTAG
AGAAGCTTCGTAGTCGTATTCTTTGAACATTTGGCTCTGGATTTTGGGTCAGACCCCTCACTCTACTTCTTTAAAAACTC
S S K H Q H K K L V N R D L K T Q S G S E M K K F L S>
                                                                191
_____HFLK1 D3_____>

      650      660      670      680      690      700      710      720
CACCTTAACTATAGATGGTGTAAACCCGGAGTGACCAAGGATTGTACACCTGTGCAGCATCCAGTGGGCTGATGACCAAGA
GTGGAATTGATATCTACCACATTGGGCCTCACTGGTTCCTAACATGTGGACACGTCGTAGGTCACCCGACTACTGGTTCCT
T L T I D G V T R S D Q G L Y T C A A S S G L M T K>
                                                                217
_____HFLK1 D3_____>

                                >Srf_Bridge_
                                |
      730      740      750      760      770      780      790      800
AGAACAGCACATTTGTCAAGGTCCATGAAAAGGGCCCGGGCGACAAACTCACACATGCCACCGTGCCAGCACCTGAA
TCTTGTCGTGTAAACAGTCCCAGGTACTTTTCCCGGGCCCGCTGTTTTGAGTGTGTACGGGTGGCAGGGTCGTGGACTT
K N S T F V R V H E K>
_____HFLK1 D3_____>
                                G P G>
                                _____>
                                D K T H T C P P C P A P E>
                                                                244
                                _____FCΔC1 (A)_____>

      810      820      830      840      850      860      870      880
CTCCTGGGGGGACCGTCAGTCTTCCCTCTTCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTAC
GAGGACCCCTTGGCAGTCAGAAGGAGAAGGGGGGTTTTGGGTTCTGTGGGAGTACTAGAGGGCCTGGGGACTCCAGTG
L L G G P S V F L F P P K P K D T L M I S R T P E V T>
                                                                271
_____FCΔC1 (A)_____>

      890      900      910      920      930      940      950      960
ATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGAGGTGCATAATG
TACGCACCACCACCTGCACTCGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATGCACCTGCCGCACCTCCACGTATTAC
C V V V D V S H E D P E V K F N W Y V D G V E V H N>
                                                                297
_____FCΔC1 (A)_____>

      970      980      990      1000      1010      1020      1030      1040
CCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCTGCACCAGGACTGG
GGTTCTGTTTCGGCGCCCTCCTCGTCATGTTGTCGTGCATGGCACACCAAGTCGCAGGAGTGGCAGGACGTGGTCTGACC
A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W>
                                                                324
_____FCΔC1 (A)_____>

```

Figure 21C

1050 1060 1070 1080 1090 1100 1110 1120
 CTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAA
 GACTTACCGTTCCTCATGTTACGTTCCAGAGGTGTTTCGGGAGGGTCGGGGGTAGCTCTTTTGGTAGAGGTTTCGGTT
 L N G K E Y K C K V S N K A L P A P I E K T I S K A K>
 351

FCAC1 (A) _____>

>A>C_A_allotype

>G>T_A_allotype

1130 1140 1150 1160 1170 1180 1190 1200
 AGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCT
 TCCCGTCGGGGCTCTTGGTGTCCACATGTGGGACGGGGGTAGGGCCCTACTCGACTGGTTCTTGGTCCAGTCGGACTGGA
 G Q P R E P Q V Y T L P P S R D E L T K N Q V S L T>
 377

FCAC1 (A) _____>

1210 1220 1230 1240 1250 1260 1270 1280
 GCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACACTACAAGACC
 CGGACCAGTTTCCGAAGATAGGGTCGCTGTAGCGGCACCTCACCTCTCGTTACCCGTCGGCCTCTTGTGATGTTCTGG
 C L V K G F Y P S D I A V E W E S N G Q P E N N Y K T>
 404

FCAC1 (A) _____>

>T>C

1290 1300 1310 1320 1330 1340 1350 1360
 ACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGG
 TCGGAGGGCAGCAGCTGAGGCTGCCGAGGAAGAAGGAGATATCGTTTCGAGTGGCACCTGTTCTCGTCCACCGTCGTCCC
 T P P V L D S D G S F F L Y S K L T V D K S R W Q Q G>
 431

FCAC1 (A) _____>

1370 1380 1390 1400 1410 1420 1430 1440
 GAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTA
 CTTGCAGAAGAGTACGAGGCACTACGTACTCCGAGACGTGTTGGTGATGTGCGTCTTCTCGGAGAGGGACAGAGGCCCAT
 N V F S C S V M H E A L H N H Y T Q K S L S L S P G>
 457

FCAC1 (A) _____>

>NotI_site

|1450

AATGAGCGGCCGC

TTACTCGCCGGCG

K *>

458

____->

Figure 22A

```

                                >EcoRI_site
                                |
      10      20      30      40      50      60      70      80
AAGCTTGGGCTGCAGGTCGATCGACTCTAGAGGATCGATCCCCGGGCGAGCTCGAATTCGCAACCACCATGGTCAGCTAC
TTCGAACCCGACGTCCAGCTAGCTGAGATCTCCTAGCTAGGGGCCGCTCGAGCTTAAGCGTTGGTGGTACCAGTCGATG
                                M V S Y>
                                1   4
                                _____>

                                >BspEI_bridge
                                |
      90      100      110      120      130      140      150      160
TGGGACACCGGGGTCCCTGCTGTGCGCGCTGCTCAGCTGTCTGCTTCTCACAGGATCTAGTTCCGGAGGTAGACCTTTTCGT
ACCCGTGTGGCCCCAGGACGACACGCGCGACGAGTCGACAGACGAAGAGTGTCTTAGATCAAGGCCTCCATCTGGAAAGCA
W D T G V L L C A L L S C L L L T G S S>
_____FLT1 SIGNAL SEQUENCE_____>
                                S G>
                                _____>
                                G R P F V>
                                31
                                _____>

      170      180      190      200      210      220      230      240
AGAGATGTACAGTGAAATCCCCGAAATTATACACATGACTGAAGGAAGGGAGCTCGTCATTCCCTGCCGGGTACGTCAC
TCTCTACATGTCACTTTAGGGGCTTTAATATGTGTACTGACTTCCTTCCCTCGAGCAGTAAGGGACGGCCCAATGCAGTG
E M Y S E I P E I I H M T E G R E L V I P C R V T S>
                                57
_____FLT1 IG DOMAIN 2_____>

      250      260      270      280      290      300      310      320
CTAACATCACTGTTACTTTAAAAAAGTTTCCACTTGACACTTTGATCCCTGATGAAAACGCATAATCTGGGACAGTAGA
GATTGTAGTGACAATGAAATTTTTCAAAGGTGAACTGTGAAACTAGGGACTACCTTTTGCGTATTAGACCCTGTCATCT
P N I T V T L K K F P L D T L I P D G K R I I W D S R>
                                84
_____FLT1 IG DOMAIN 2_____>

      330      340      350      360      370      380      390      400
AAGGGCTTCATCATATCAAATGCAACGTACAAAGAAATAGGGCTTCTGACCTGTGAAGCAACAGTCAATGGGCATTTGTA
TTCCCGAAGTAGTATAGTTTACGTTGCATGTTTCTTTATCCCGAAGACTGGACACTTCGTTGTCAGTTACCCGTAAACAT
K G F I I S N A T Y K E I G L L T C E A T V N G H L Y>
                                111
_____FLT1 IG DOMAIN 2_____>

      410      420      430      440      450      460      470      480
TAAGACAAACTATCTCACACATCGACAAACCAATACAATCATAGATATCCAGCTGTTGCCAGGAAGTCGCTGGAGCTGC
ATTCTGTTTGTAGAGTGTGTAGCTGTTTGGTTATGTTAGTATCTATAGGTCGACAACGGGTCCTTCAGCGACCTCGACG
K T N Y L T H R Q T N T I I D>
_____FLT1 IG DOMAIN 2_____>
                                I Q L L P R K S L E L>
                                137
_____VEGFR3 (FLT4) IG DOMAIN 3_____>

```

Figure 22B

490 500 510 520 530 540 550 560
TGGTAGGGGAGAAGCTGGTCCTCAACTGCACCGTGTGGGCTGAGTTTAACTCAGGTGTCACCTTTGACTGGGACTACCCA
ACCATCCCCCTCTTCGACCAGGAGTTGACGTGGCACACCCGACTCAAATTGAGTCCACAGTGGAAACTGACCCTGATGGGT
L V G E K L V L N C T V W A E F N S G V T F D W D Y P>
164
____VEGFR3 (FLT4) IG DOMAIN 3____>

570 580 590 600 610 620 630 640
GGGAAGCAGGCAGAGCGGGGTAAAGTGGGTGCCCCGAGCGACGCTCCCAACAGACCCACACAGAACTCTCCAGCATCCTGAC
CCCTTCGTCCGTCTCGCCCCATTACCCACGGGCTCGCTGCGAGGGTTGTCTGGGTGTGTCTTGAGAGGTCGTAGGACTG
G K Q A E R G K W V P E R R S Q Q T H T E L S S I L T>
191
____VEGFR3 (FLT4) IG DOMAIN 3____>

650 660 670 680 690 700 710 720
CATCCACAACGTCAGCCAGCACGACCTGGGCTCGTATGTGTGCAAGGCCAACACGGCATCCAGCGATTTCGGGAGAGCA
GTAGGTGTTGCAGTCGGTCGTGCTGGACCCGAGCATAACACAGTTCCGGTTGTTGCCGTAGGTCGCTAAAGCCCTCTCGT
I H N V S Q H D L G S Y V C K A N N G I Q R F R E S>
217
____VEGFR3 (FLT4) IG DOMAIN 3____>

730 740 750 760 770 780 790 800
CCGAGGTCAATTGTGCATGAAAATGGCCCGGGCGACAAACTCACACATGCCACCGTGCCAGCACCTGAACTCCTGGGG
GGCTCCAGTAACACGTACTTTTACCGGGCCCGCTGTTTTGAGTGTGTACGGGTGGCACGGGTCGTGGACTTGAGGACCCC
T E V I V H E N>
____VEGFR3 (FLT4) IG____>
G P G>
____>
D K T H T C P P C P A P E L L G>
244
____FCΔC1 - A ALLOTYPE____>

810 820 830 840 850 860 870 880
GGACCGTCAGTCTTCCTCTTCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGT
CCTGGCAGTCAGAAGGAGAAGGGGGGTTTGGGTTCTGTGGGAGTACTAGAGGGCCTGGGGACTCCAGTGTACGCACCA
G P S V F L F P P K P K D T L M I S R T P E V T C V V>
271
____FCΔC1 - A ALLOTYPE____>

890 900 910 920 930 940 950 960
GGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAA
CCACCTGCACTCGGTGCTTCTGGGACTCCAGTTCAAGTTGACCATGCACCTGCCGCACCTCCACGTATTACGGTTCTGTT
V D V S H E D P E V K F N W Y V D G V E V H N A K T>
297
____FCΔC1 - A ALLOTYPE____>

970 980 990 1000 1010 1020 1030 1040
AGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCTCACCCTGACCCAGGACTGGCTGAATGGC
TCGGCGCCCTCCTCGTCATGTTGTGCTGCATGGCACACCAGTCGCAGGAGTGGCAGGACGTGGTCTTGACCGACTTACCG
K P R E E Q Y N S T Y R V V S V L T V L H Q D W L N G>
324
____FCΔC1 - A ALLOTYPE____>

```
      1050       1060       1070       1080       1090       1100       1110       1120  
AAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCAAAGCCAAAGGGCAGCC  
TTCTTCATGTTTACGTTCCAGAGGTTGTTTTCGGGAGGGTCGGGGTAGCTCTTTTGGTAGAGGTTTCGGTTTCCCGTCGG  
K E Y K C K V S N K A L P A P I E K T I S K A K G Q P>  
  
                                     FCΔC1 - A ALLOTYPE
```

351

```
>A>C_A_allotype  
|  
>G>T_A_allotype  
|   |  
    |   |  
1130     1140     1150     1160     1170     1180     1190     1200  
CCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCA  
GGCTCTTGGTGTCCACATGTGGGACGGGGGTAGGGCCCTACTCGACTGGTTCTTGGTCCAGTCGGACTGGACGGACCAGT  
R E P Q V Y T L P P S R D E L T K N Q V S L T C L V>
```

377

```
FCΔC1 - A ALLOTYPE
```

```
      1210       1220       1230       1240       1250       1260       1270       1280  
AAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAATAACAAGACCACGCCTCCC  
TTCCGAAGATAGGGTCGCTGTAGCGGCACCTCACCTCTCGTTACCCGTCGGCCTCTTGTTGATGTTCTGGTGCGGAGGG  
K G F Y P S D I A V E W E S N G Q P E N N Y K T T P P>
```

404

```
FCΔC1 - A ALLOTYPE
```

```
>T>C  
|  
1290     1300     1310     1320     1330     1340     1350     1360  
GTGCTGGACTCCGACGGCTCCTTCTTCTTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTT  
CACGACCTGAGGCTGCCGAGGAAGAAGGAGATATCGTTGAGTGGCACCTGT'TCTCGTCCACCGTCGTCCCCTTGCAGAA  
V L D S D G S F F L Y S K L T V D K S R W Q Q G N V F>
```

431

```
FCΔC1 - A ALLOTYPE
```

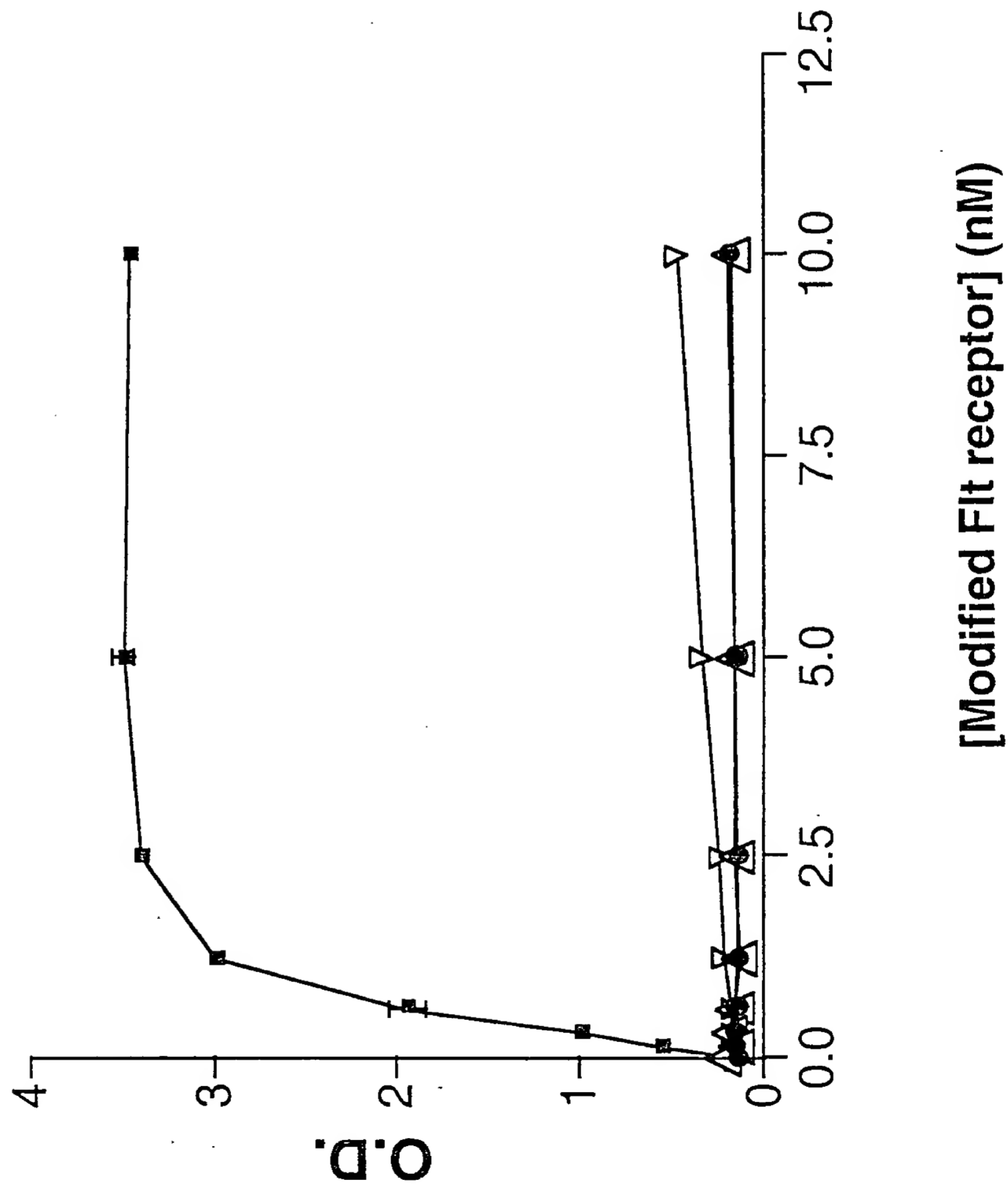
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>NotI_site  
|  
1370     1380     1390     1400     1410     1420     1430     1440  
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GAGTACGAGGCACTACGTACTCCGAGACGTGTTGGTGTATGTGCGTCTTCTCGGAGAGGGACAGAGGCCATTACTCGCC  
S C S V M H E A L H N H Y T Q K S L S L S P G K *>
```

455

```
FCΔC1 - A ALLOTYPE
```

CCGC
GGCG

Figure 23



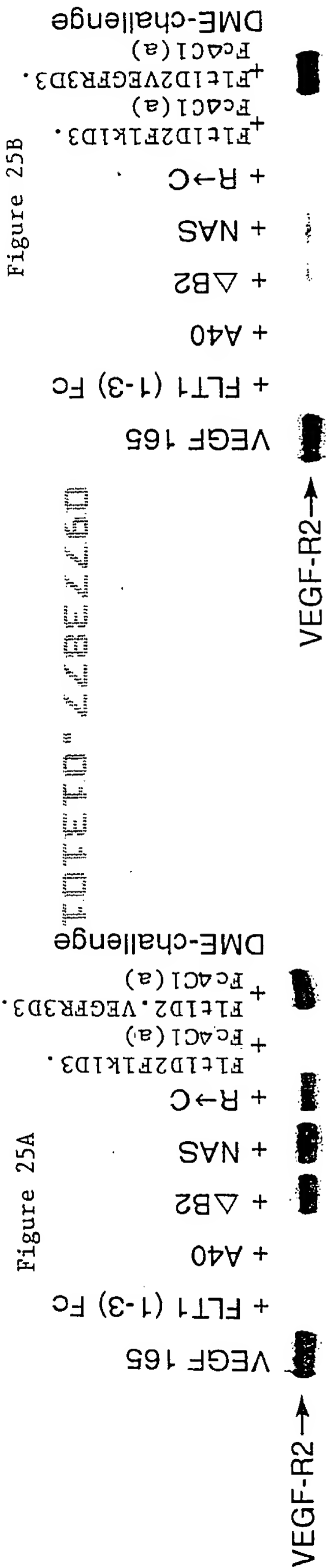
COLORED PEOPLE

COLORED PEOPLE

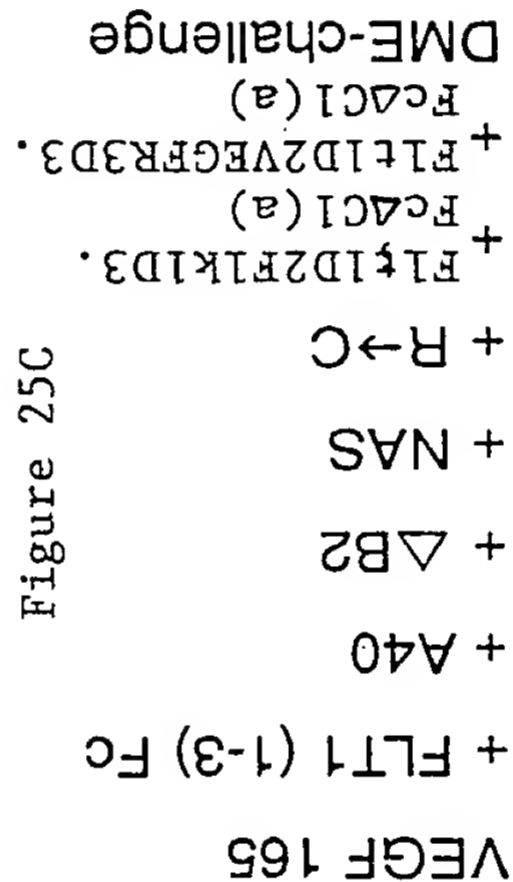
430 *					440 *					450 *					460 *					470 *					480 *				
TCT	GTT	GGA	GAA	AAG	CTT	GTC	TTA	AAT	TGT	ACA	GCA	AGA	ACT	GAA	CTA	AAT	GTG	GGG	ATT										
AGA	CAA	CCT	CTT	TTC	GAA	CAG	AAT	TTA	ACA	TGT	CGT	TCT	TGA	CTT	GAT	TTA	CAC	CCC	TAA										
S	V	G	E	K	L	V	L	N	C	T	A	R	T	E	L	N	V	G	I	>									
141_____145_____					hFLK1 IG DOMAIN 3_____					155_____					160>														
490 *					500 *					510 *					520 *					530 *					540 *				
GAC	TTC	AAC	TGG	GAA	TAC	CCT	TCT	TCG	AAG	CAT	CAG	CAT	AAG	AAA	CTT	GTA	AAC	CGA	GAC										
CTG	AAG	TTG	ACC	CTT	ATG	GGA	AGA	AGC	TTC	GTA	GTC	GTA	TTC	TTT	GAA	CAT	TTG	GCT	CTG										
D	F	N	W	E	Y	P	S	S	K	H	Q	H	K	K	L	V	N	R	D	>									
161_____165_____					hFLK1 IG DOMAIN 3_____					175_____					180>														
550 *					560 *					570 *					580 *					590 *					600 *				
CTA	AAA	ACC	CAG	TCT	GGG	AGT	GAG	ATG	AAG	AAA	TTT	TTG	AGC	ACC	TTA	ACT	ATA	GAT	GGT										
GAT	TTT	TGG	GTC	AGA	CCC	TCA	CTC	TAC	TTC	TTT	AAA	AAC	TCG	TGG	AAT	TGA	TAT	CTA	CCA										
L	K	T	Q	S	G	S	E	M	K	K	F	L	S	T	L	T	I	D	G	>									
181_____185_____					hFLK1 IG DOMAIN 3_____					195_____					200>														
610 *					620 *					630 *					640 *					650 *					660 *				
GTA	ACC	CGG	AGT	GAC	CAA	GGA	TTG	TAC	ACC	TGT	GCA	GCA	TCC	AGT	GGG	CTG	ATG	ACC	AAG										
CAT	TGG	GCC	TCA	CTG	GTT	CCT	AAC	ATG	TGG	ACA	CGT	CGT	AGG	TCA	CCC	GAC	TAC	TGG	TTC										
V	T	R	S	D	Q	G	L	Y	T	C	A	A	S	S	G	L	M	T	K	>									
201_____205_____					hFLK1 IG DOMAIN 3_____					215_____					220>														
670 *					680 *					690 *					700 *					710 *					720 *				
AAG	AAC	AGC	ACA	TTT	GTC	AGG	GTC	CAT	GAA	AAG	GAC	AAA	ACT	CAC	ACA	TGC	CCA	CCG	TGC										
TTC	TTG	TCG	TGT	AAA	CAG	TCC	CAG	GTA	CTT	TTC	CTG	TTT	TGA	GTG	TGT	ACG	GGT	GGC	ACG										
K	N	S	T	F	V	R	V	H	E	K										>									
221_____hFLK1 IG DOMAIN 3_____					231>					D K T H T C P P C>					232_____hFCAC1 A _____240>														
730 *					740 *					750 *					760 *					770 *					780 *				
CCA	GCA	CCT	GAA	CTC	CTG	GGG	GGA	CCG	TCA	GTC	TTC	CTC	TTC	CCC	CCA	AAA	CCC	AAG	GAC										
GGT	CGT	GGA	CTT	GAG	GAC	CCC	CCT	GGC	AGT	CAG	AAG	GAG	AAG	GGG	GGT	TTT	GGG	TTC	CTG										
P	A	P	E	L	L	G	G	P	S	V	F	L	F	P	P	K	P	K	D	>									
241_____245_____					hFCAC1 A _____					255_____					260>														
790 *					800 *					810 *					820 *					830 *					840 *				
ACC	CTC	ATG	ATC	TCC	CGG	ACC	CCT	GAG	GTC	ACA	TGC	GTG	GTG	GTG	GAC	GTG	AGC	CAC	GAA										
TGG	GAG	TAC	TAG	AGG	GCC	TGG	GGA	CTC	CAG	TGT	ACG	CAC	CAC	CAC	CTG	CAC	TCG	GTG	CTT										
T	L</																												

Figure 24C

910	920	930	940	950	960
*	*	*	*	*	*
AAG CCG CGG GAG GAG CAG TAC AAC AGC ACG TAC CGT GTG GTC AGC GTC CTC ACC GTC CTG					
TTC GGC GCC CTC CTC GTC ATG TTG TCG TGC ATG GCA CAC CAG TCG CAG GAG TGG CAG GAC					
K P R E E Q Y N S T Y R V V S V L T V L>					
301_____305_____hFCAC1 A _____315_____320>					
970	980	990	1000	1010	1020
*	*	*	*	*	*
CAC CAG GAC TGG CTG AAT GGC AAG GAG TAC AAG TGC AAG GTC TCC AAC AAA GCC CTC CCA					
GTG GTC CTG ACC GAC TTA CCG TTC CTC ATG TTC ACG TTC CAG AGG TTG TTT CGG GAG GGT					
H Q D W L N G K E Y K C K V S N K A L P>					
321_____325_____hFCAC1 A _____335_____340>					
1030	1040	1050	1060	1070	1080
*	*	*	*	*	*
GCC CCC ATC GAG AAA ACC ATC TCC AAA GCC AAA GGG CAG CCC CGA GAA CCA CAG GTG TAC					
CGG GGG TAG CTC TTT TGG TAG AGG TTT CGG TTT CCC GTC GGG GCT CTT GGT GTC CAC ATG					
A P I E K T I S K A K G Q P R E P Q V Y>					
341_____345_____hFCAC1 A _____355_____360>					
1090	1100	1110	1120	1130	1140
*	*	*	*	*	*
ACC CTG CCC CCA TCC CGG GAT GAG CTG ACC AAG AAC CAG GTC AGC CTG ACC TGC CTG GTC					
TGG GAC GGG GGT AGG GCC CTA CTC GAC TGG TTC TTG GTC CAG TCG GAC TGG ACG GAC CAG					
T L P P S R D E L T K N Q V S L T C L V>					
361_____365_____hFCAC1 A _____375_____380>					
1150	1160	1170	1180	1190	1200
*	*	*	*	*	*
AAA GGC TTC TAT CCC AGC GAC ATC GCC GTG GAG TGG GAG AGC AAT GGG CAG CCG GAG AAC					
TTT CCG AAG ATA GGG TCG CTG TAG CGG CAC CTC ACC CTC TCG TTA CCC GTC GGC CTC TTG					
K G F Y P S D I A V E W E S N G Q P E N>					
381_____385_____hFCAC1 A _____395_____400>					
1210	1220	1230	1240	1250	1260
*	*	*	*	*	*
AAC TAC AAG ACC ACG CCT CCC GTG CTG GAC TCC GAC GGC TCC TTC TTC CTC TAC AGC AAG					
TTG ATG TTC TGG TGC GGA GGG CAC GAC CTG AGG CTG CCG AGG AAG AAG GAG ATG TCG TTC					
N Y K T T P P V L D S D G S F F L Y S K>					
401_____405_____hFCAC1 A _____415_____420>					
1270	1280	1290	1300	1310	1320
*	*	*	*	*	*
CTC ACC GTG GAC AAG AGC AGG TGG CAG CAG GGG AAC GTC TTC TCA TGC TCC GTG ATG CAT					
GAG TGG CAC CTG TTC TCG TCC ACC GTC GTC CCC TTG CAG AAG AGT ACG AGG CAC TAC GTA					
L T V D K S R W Q Q G N V F S C S V M H>					
421_____425_____hFCAC1 A _____435_____440>					
1330	1340	1350	1360	1370	
*	*	*	*	*	
GAG GCT CTG CAC AAC CAC TAC ACG CAG AAG AGC CTC TCC CTG TCT CCG GGT AAA TGA					
CTC CGA GAC GTG TTG GTG ATG TGC GTC TTC TCG GAG AGG GAC AGA GGC CCA TTT ACT					
E A L H N H Y T Q K S L S L S P G K *>					
441_____445_____hFCAC1 A _____455_____458>					



1.5 Fold Modified
Flt1 receptor



3.0 Fold Modified
Flt1 receptor

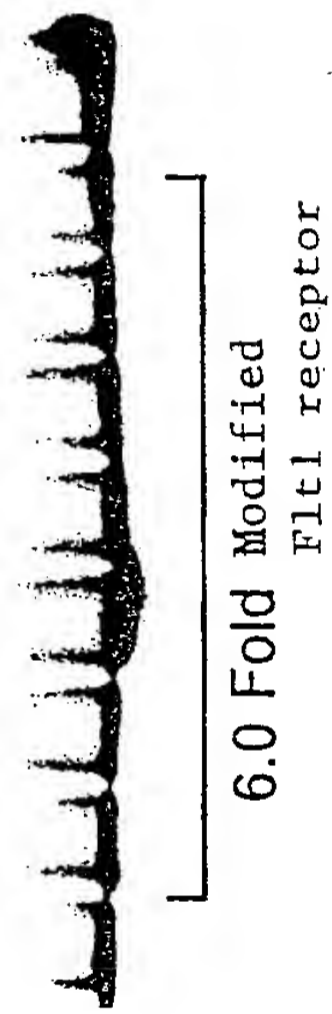


Figure 26B

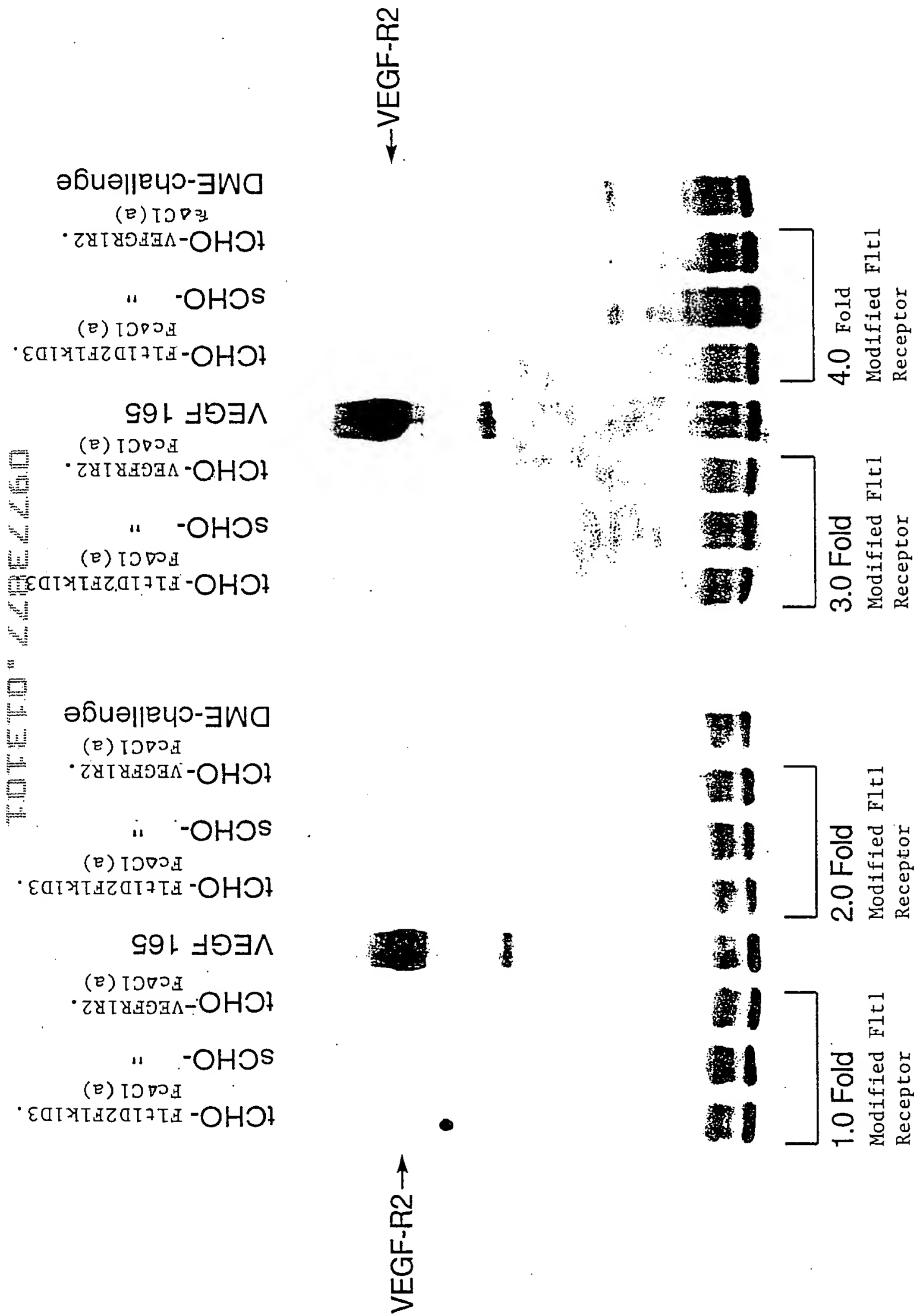


Figure 26A

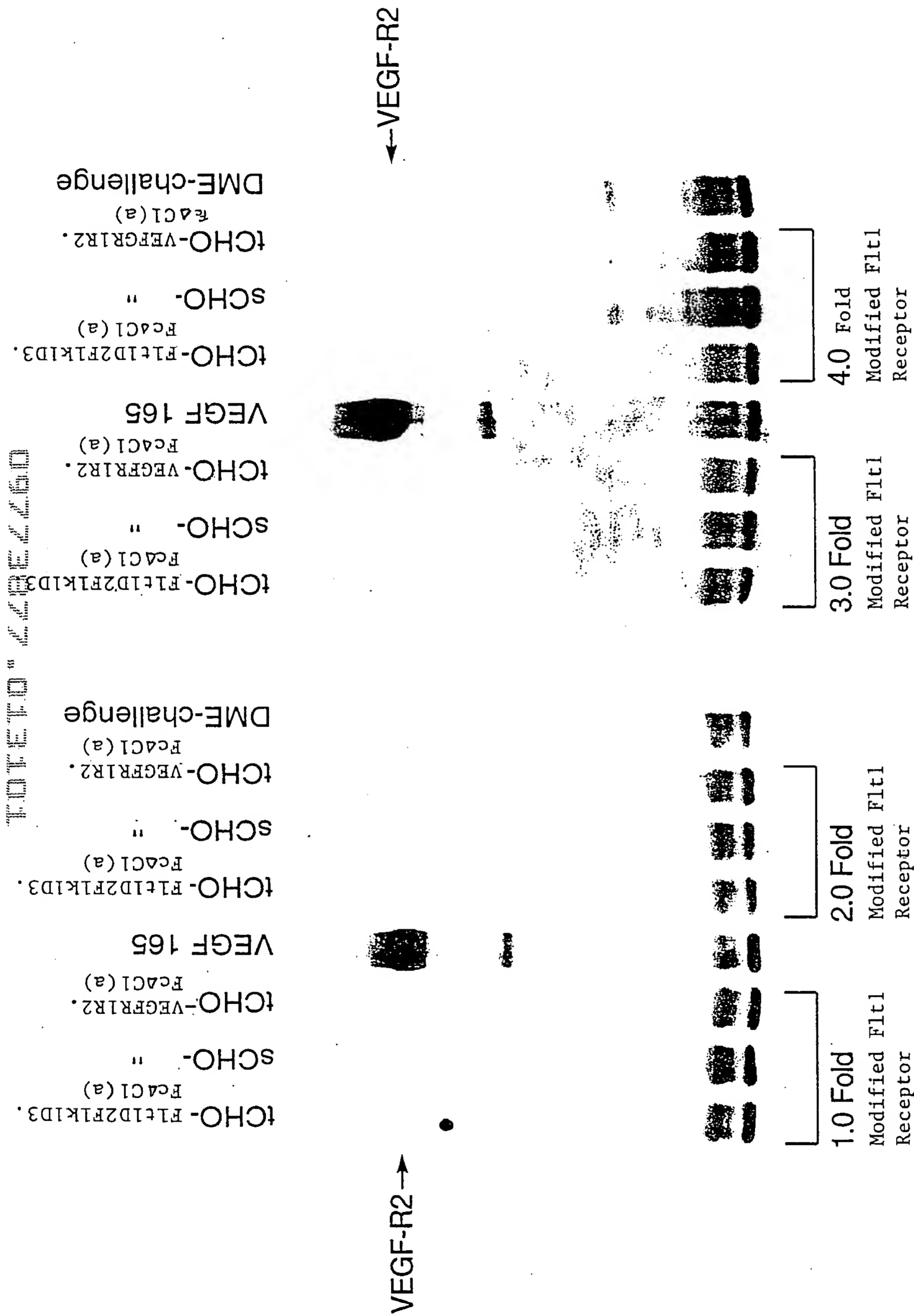


Figure 27

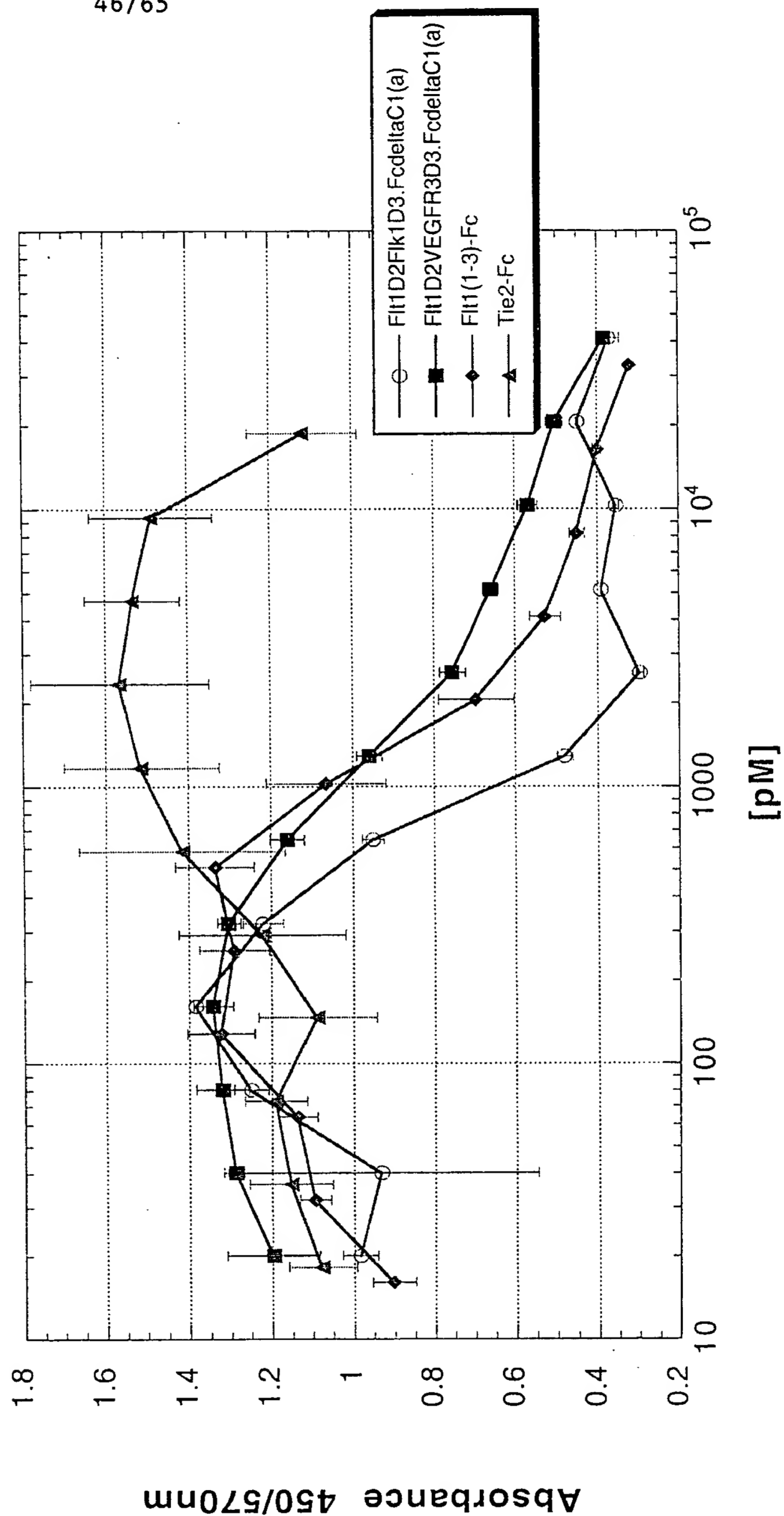


Figure 28

Binding Stoichiometry of hVEGF165 to F1t1D2F1k1D3.Fc4C1(a) & VEGFR1R2-Fc4C1(a)		
hVEGF165 (nM)	VEGF/F1t1D2F1k1D3.Fc4C1(a)	VEGF/VEGFR1R2-Fc4C1(a)
1	0.93	0.98
10	0.97	0.94
50	1	0.99
Average±StDev	0.96±0.03	0.97±0.02

Figure 29

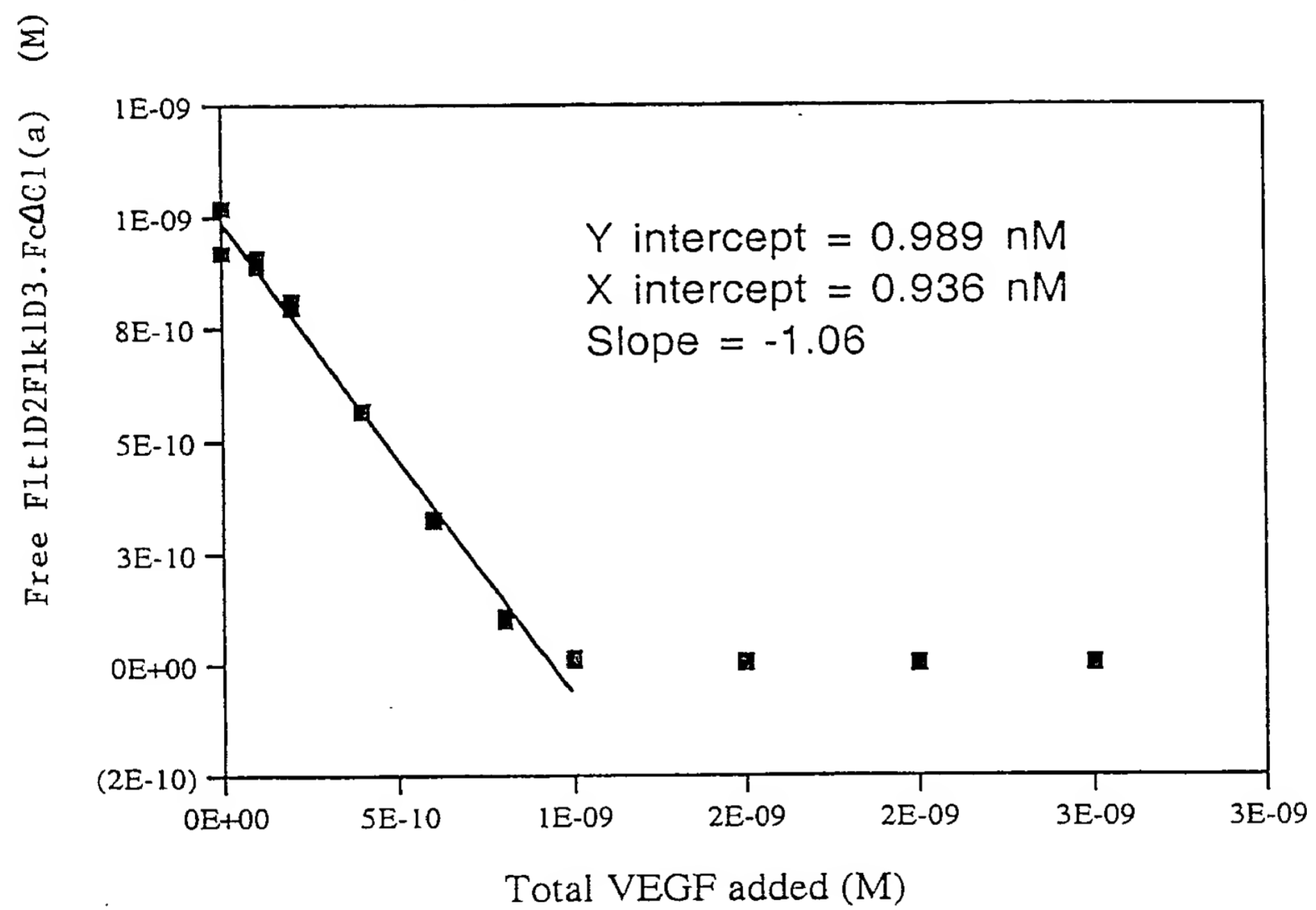


Figure 30

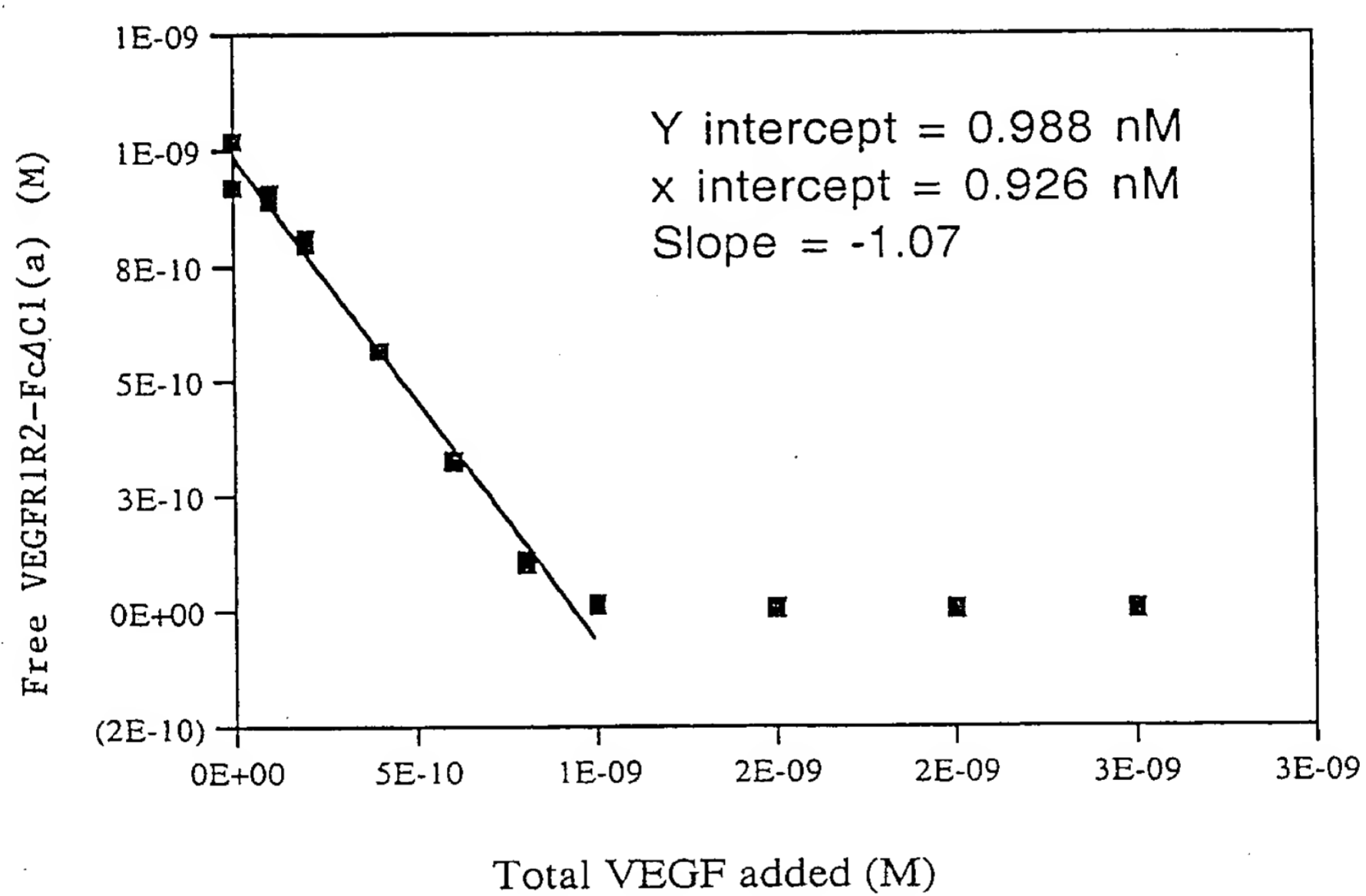


Figure 31

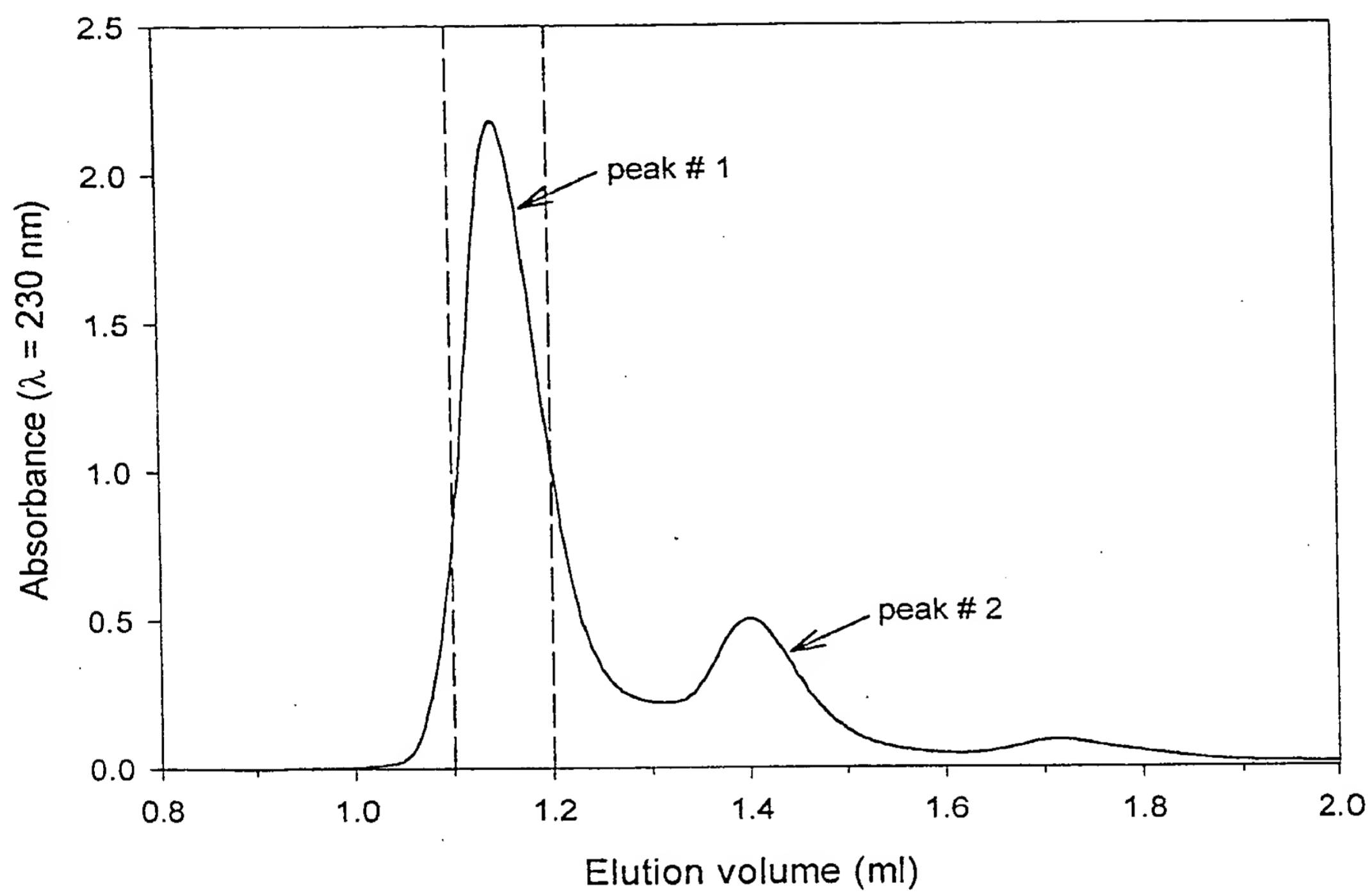


Figure 32

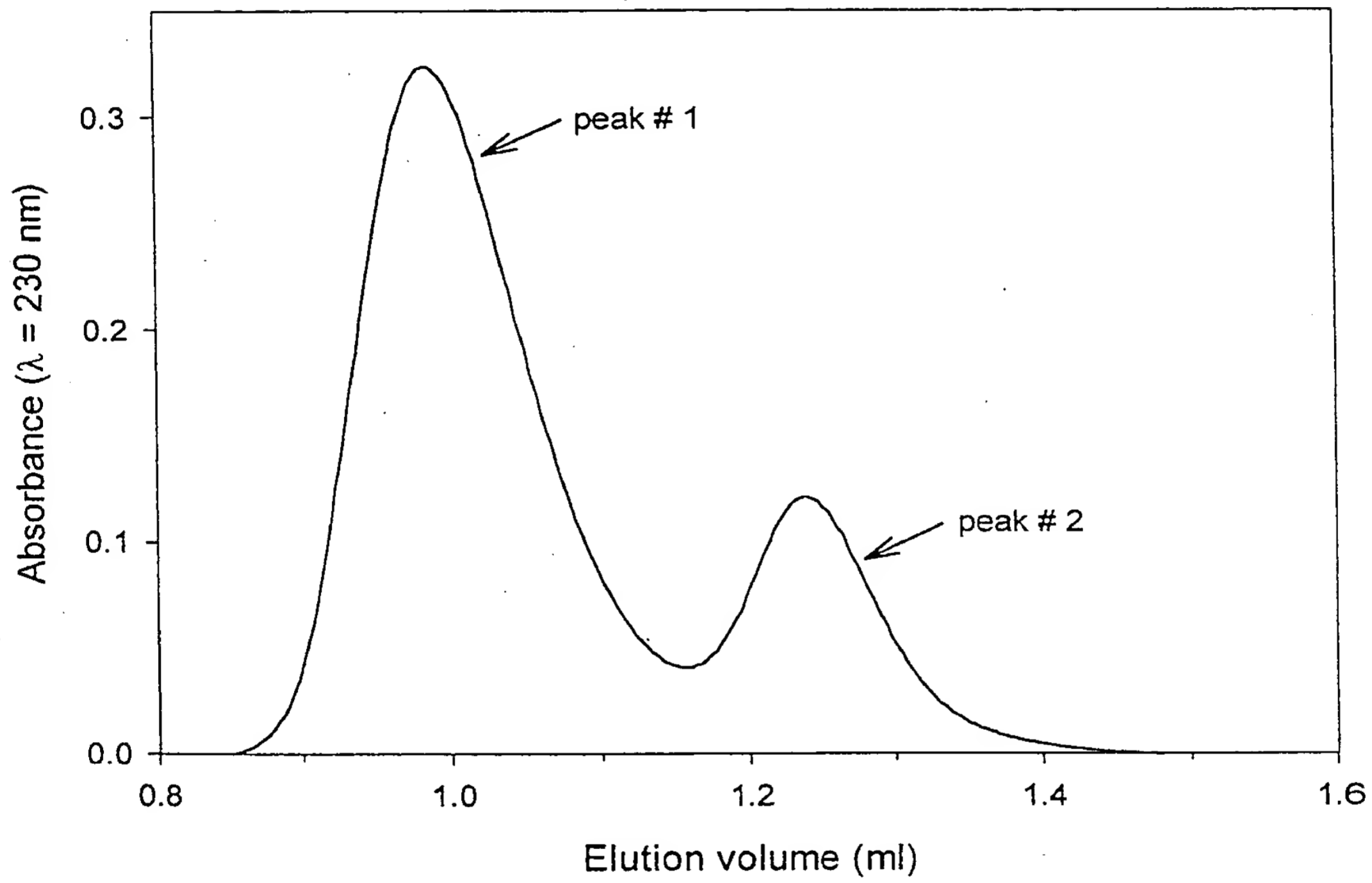


Figure 33

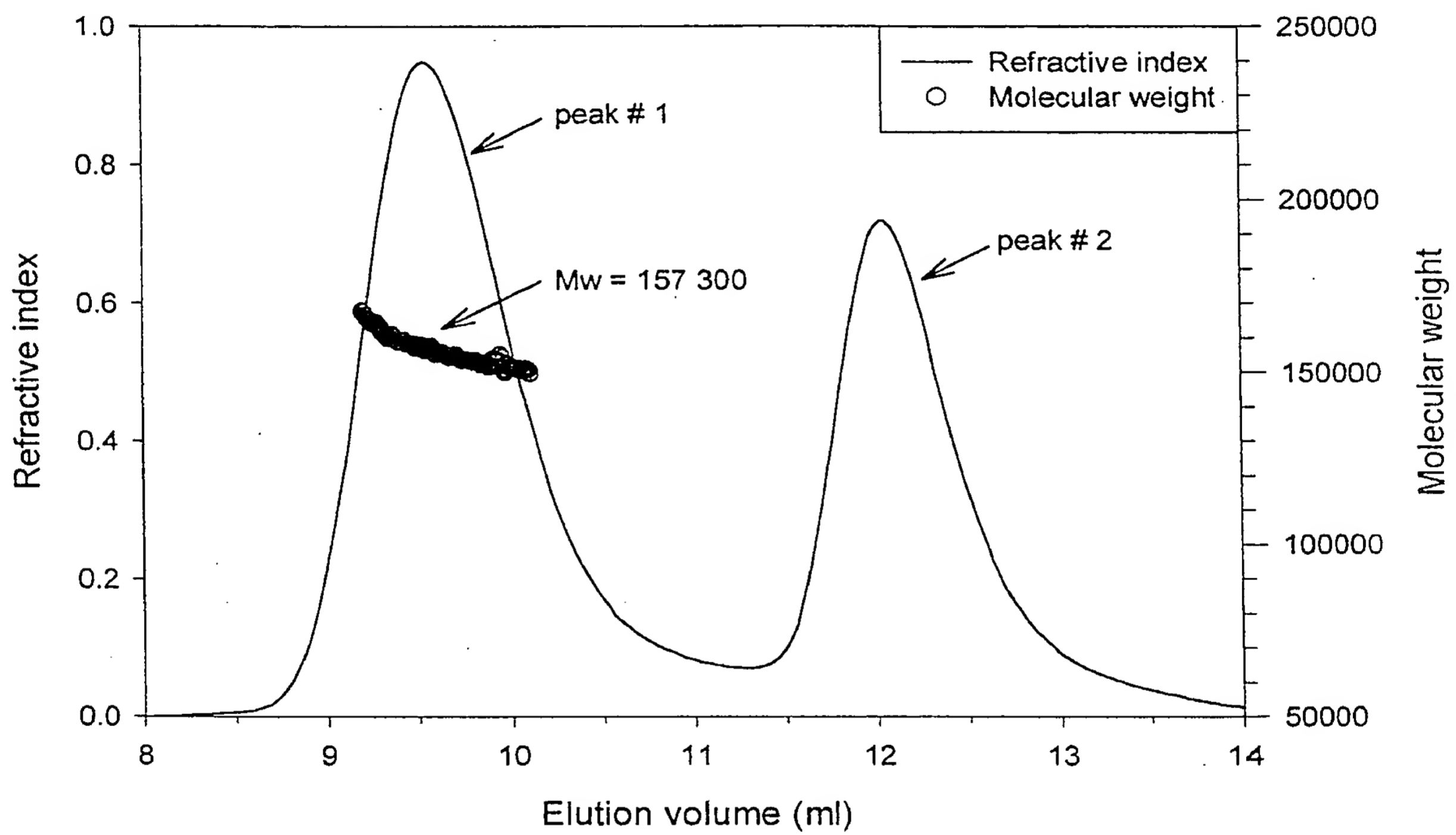


Figure 34

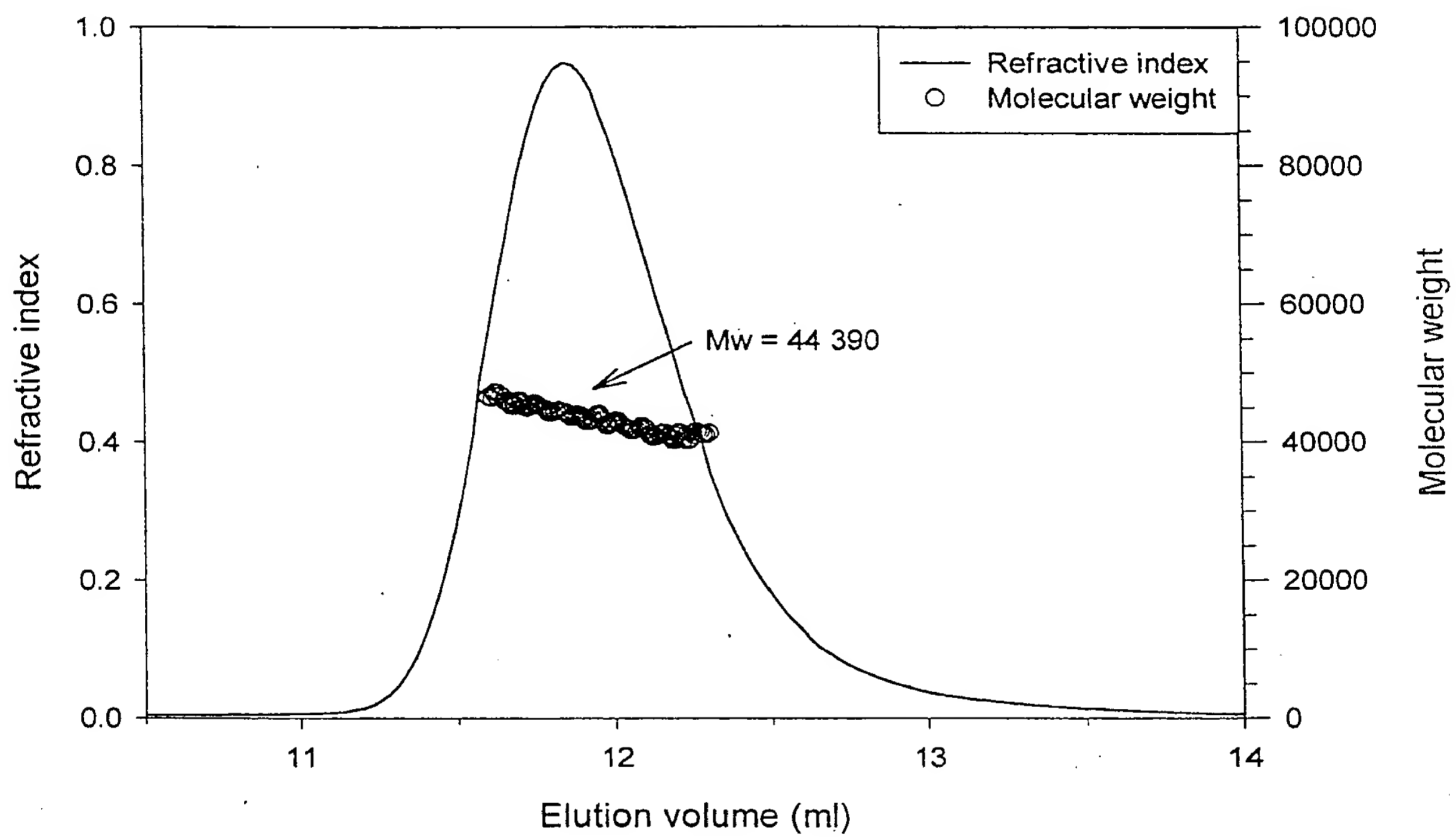


Figure 35

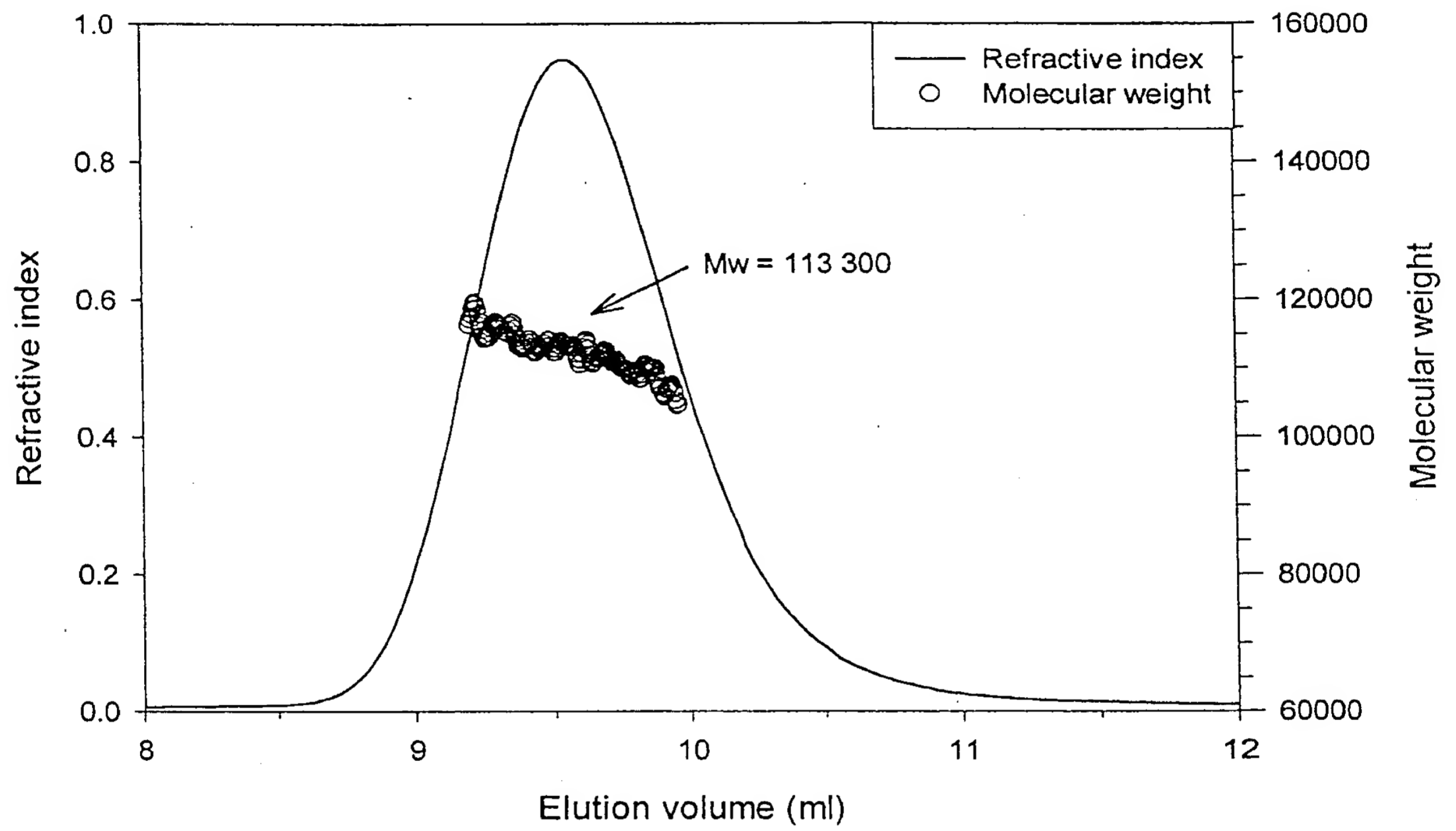


Figure 36

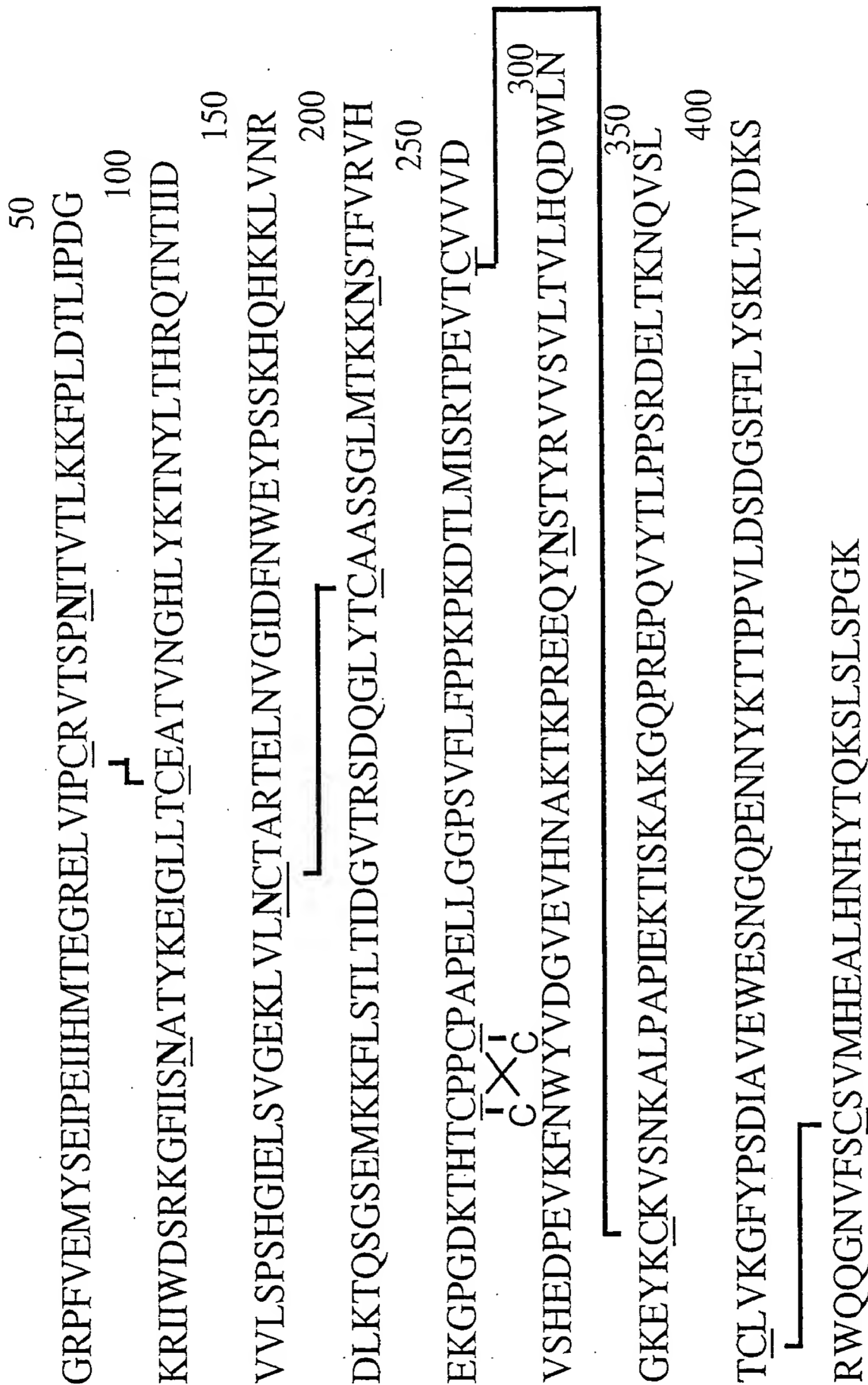


Figure 38

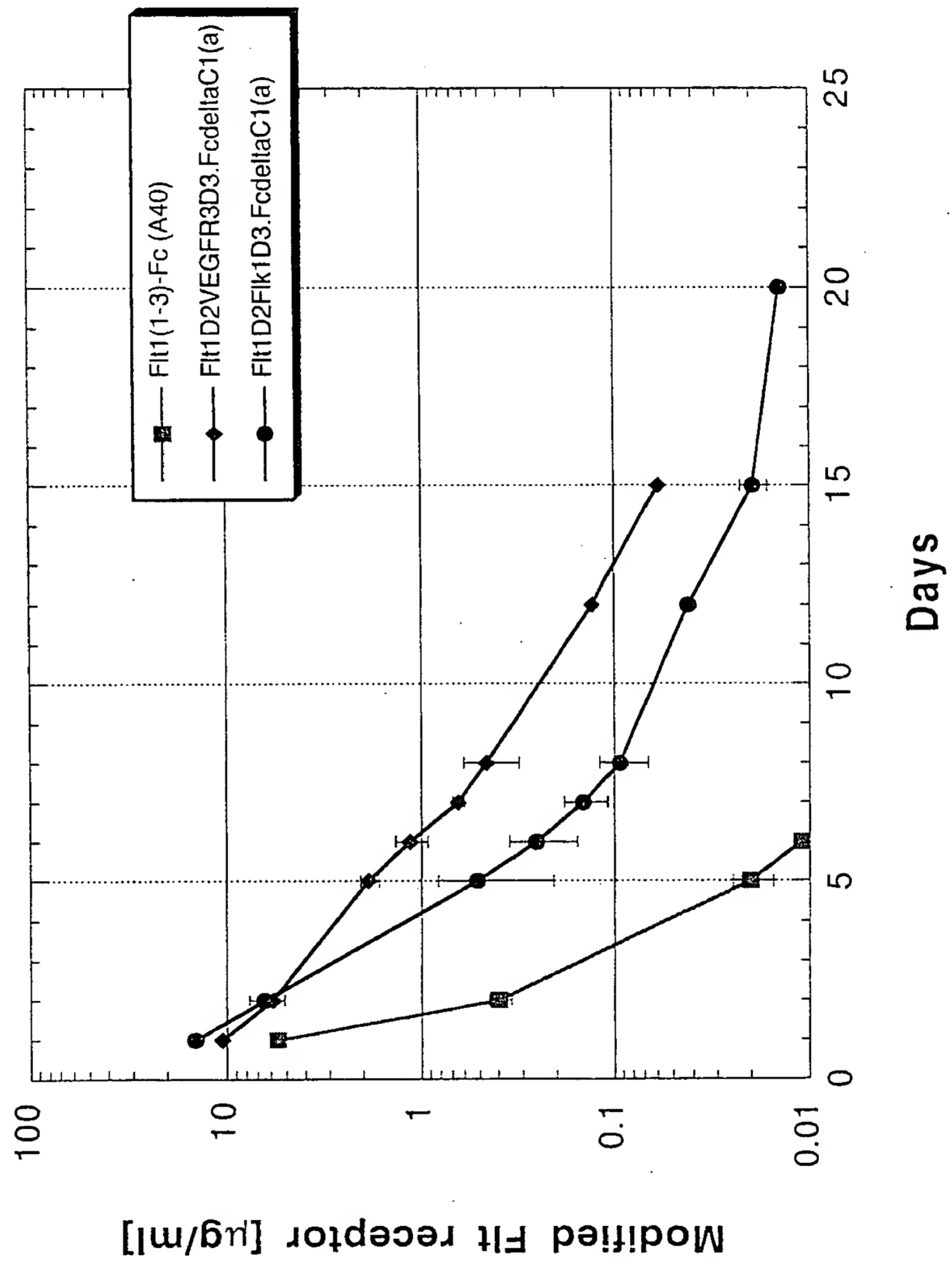


Figure 39

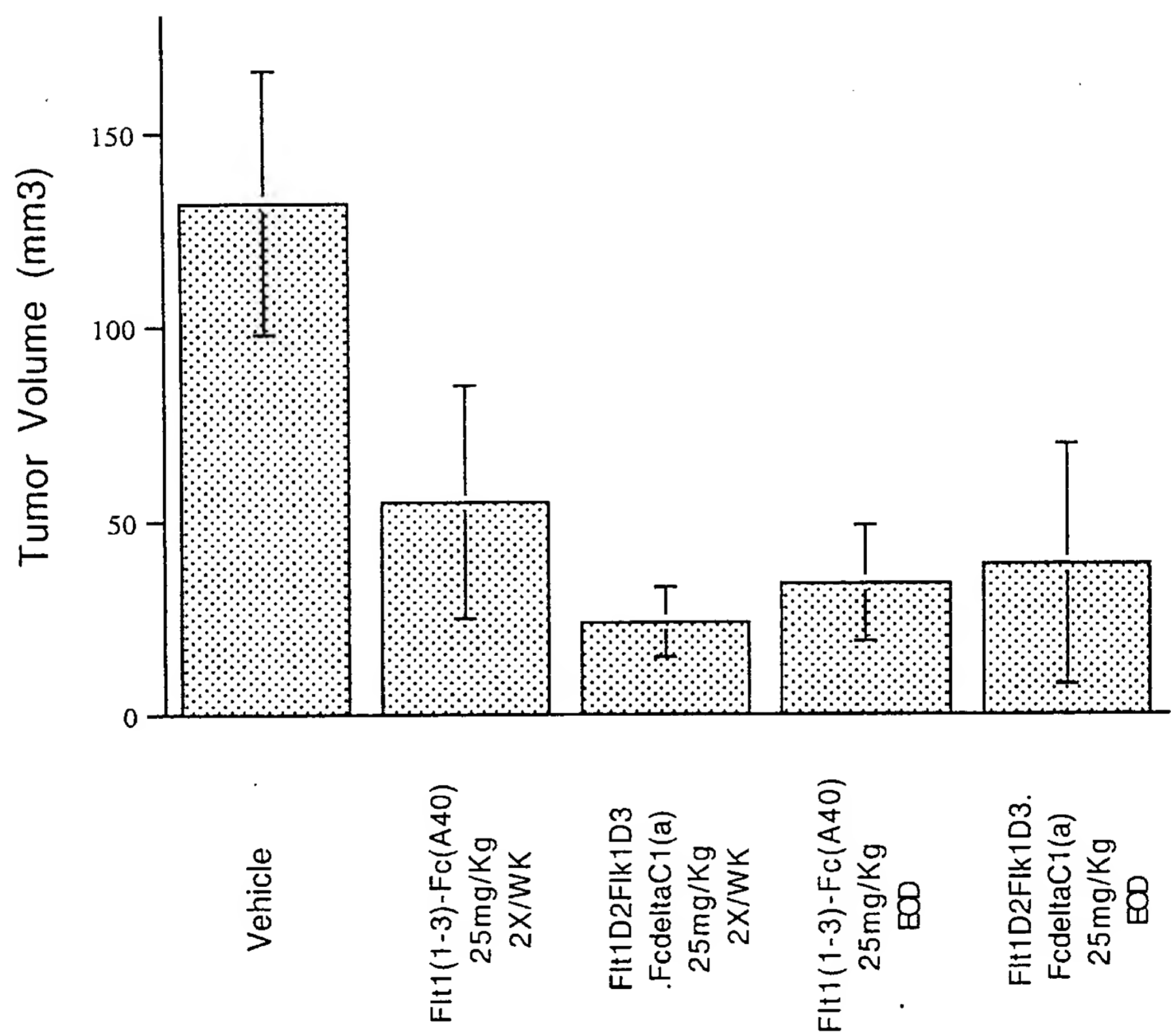


Figure 40

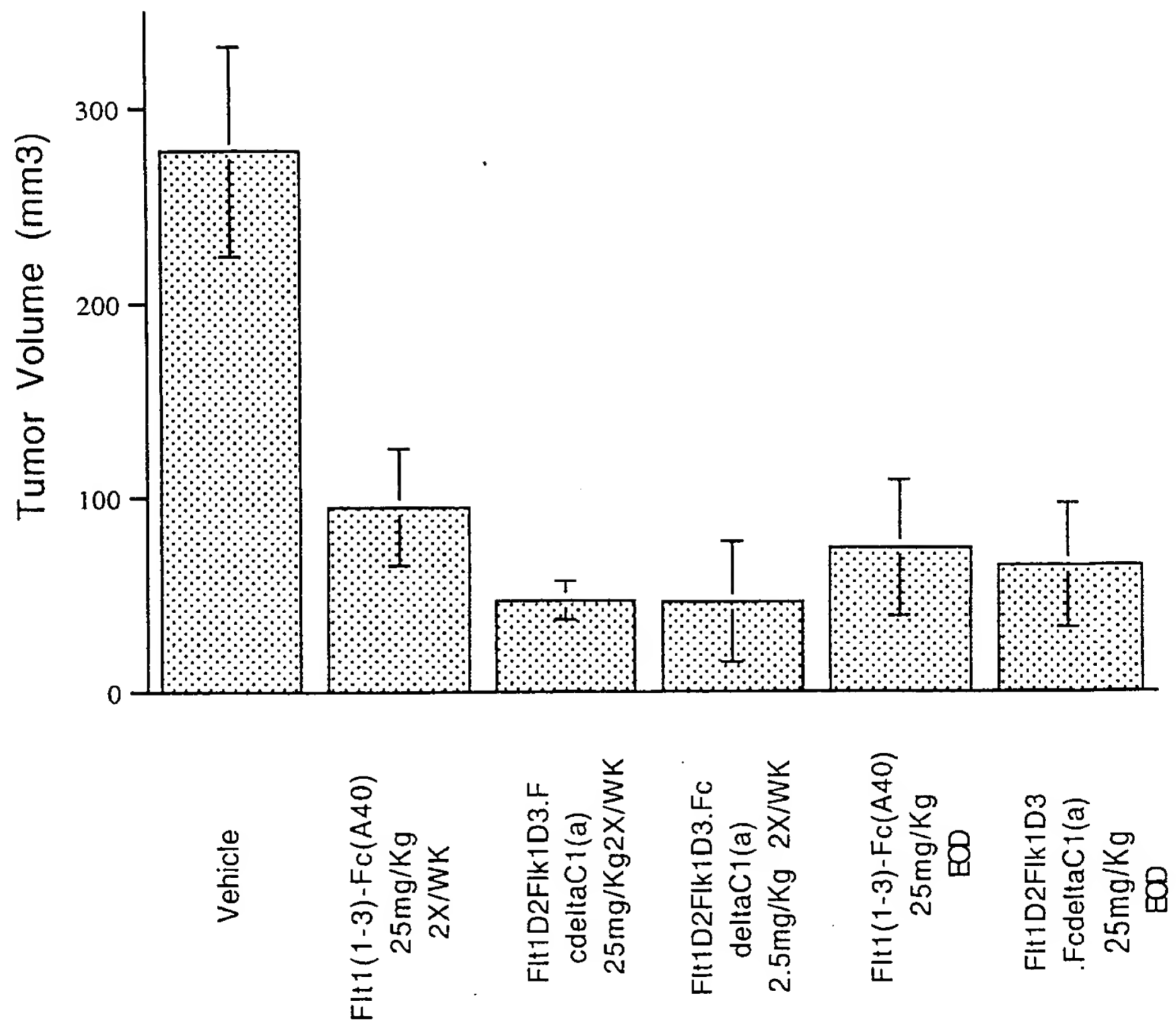


Figure 41

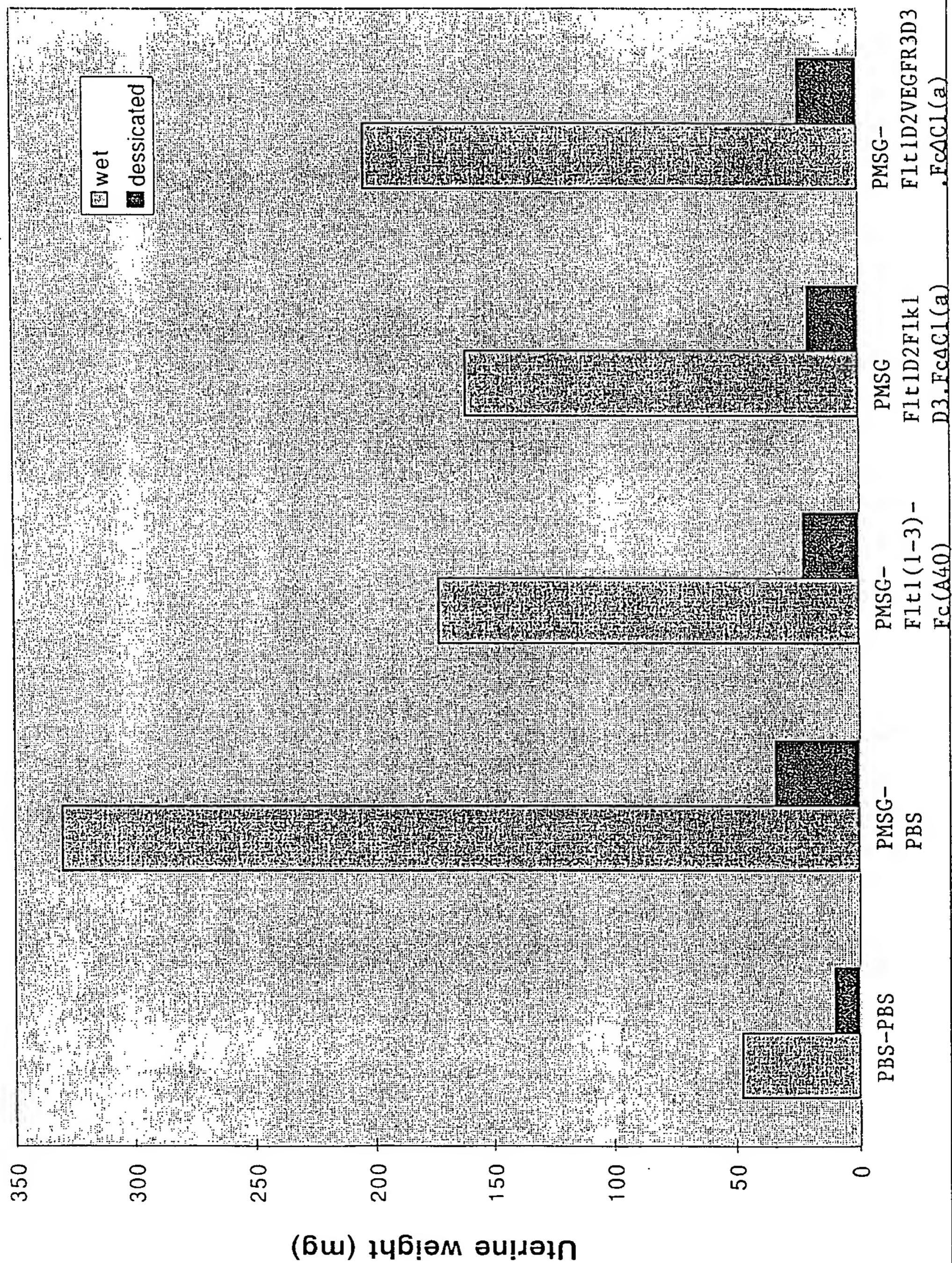


Figure 42A

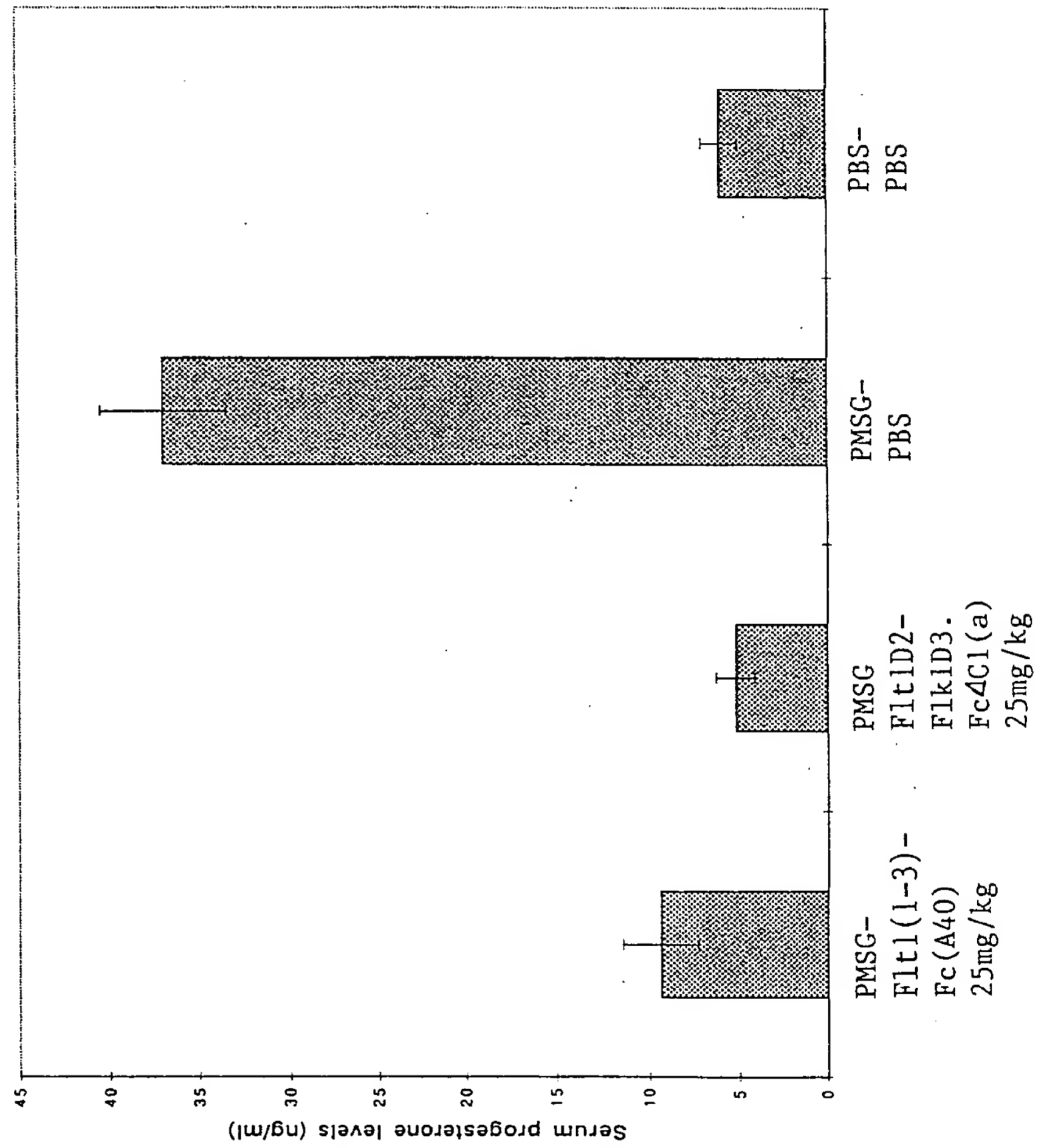


Figure 42B

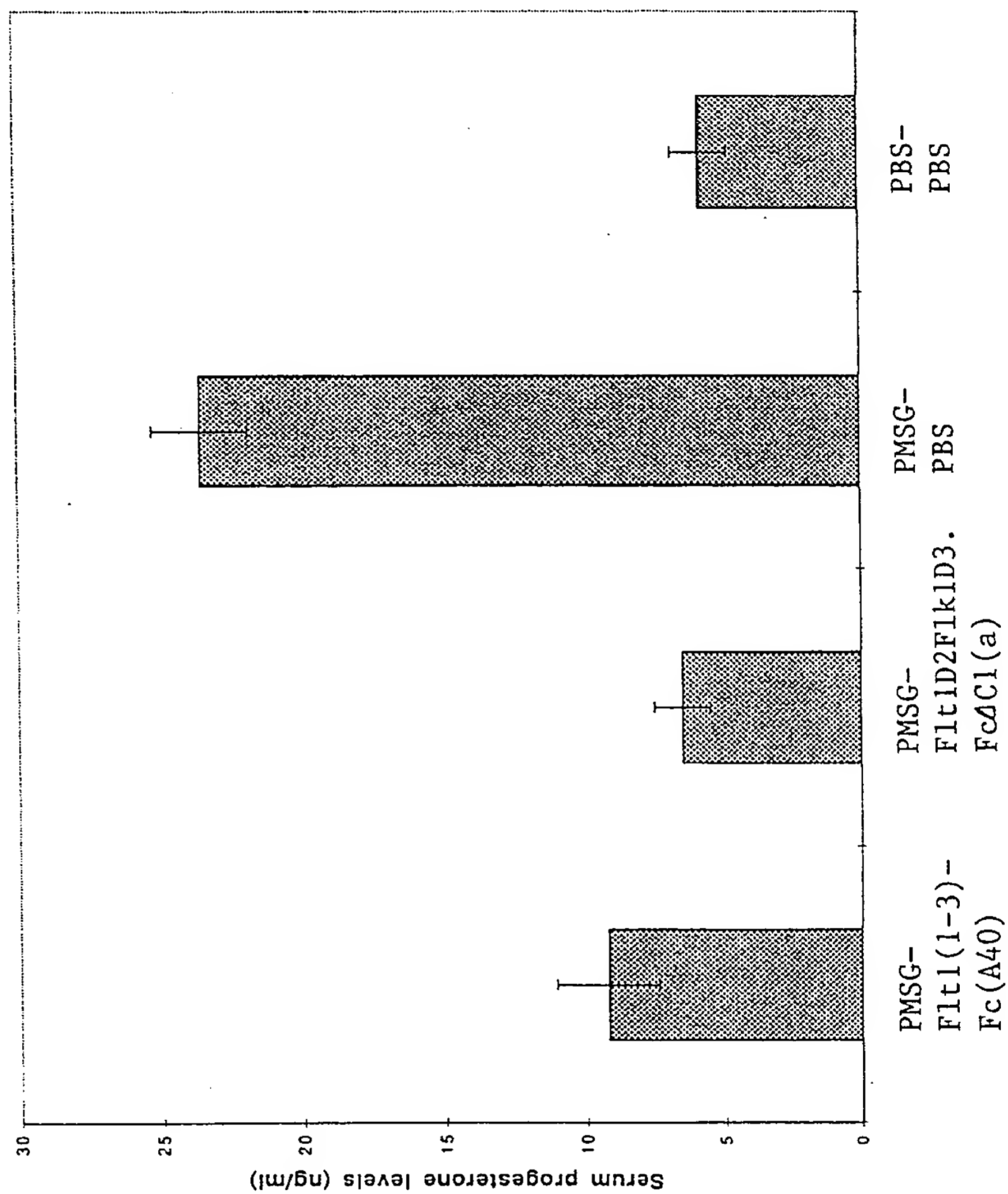


Fig.43

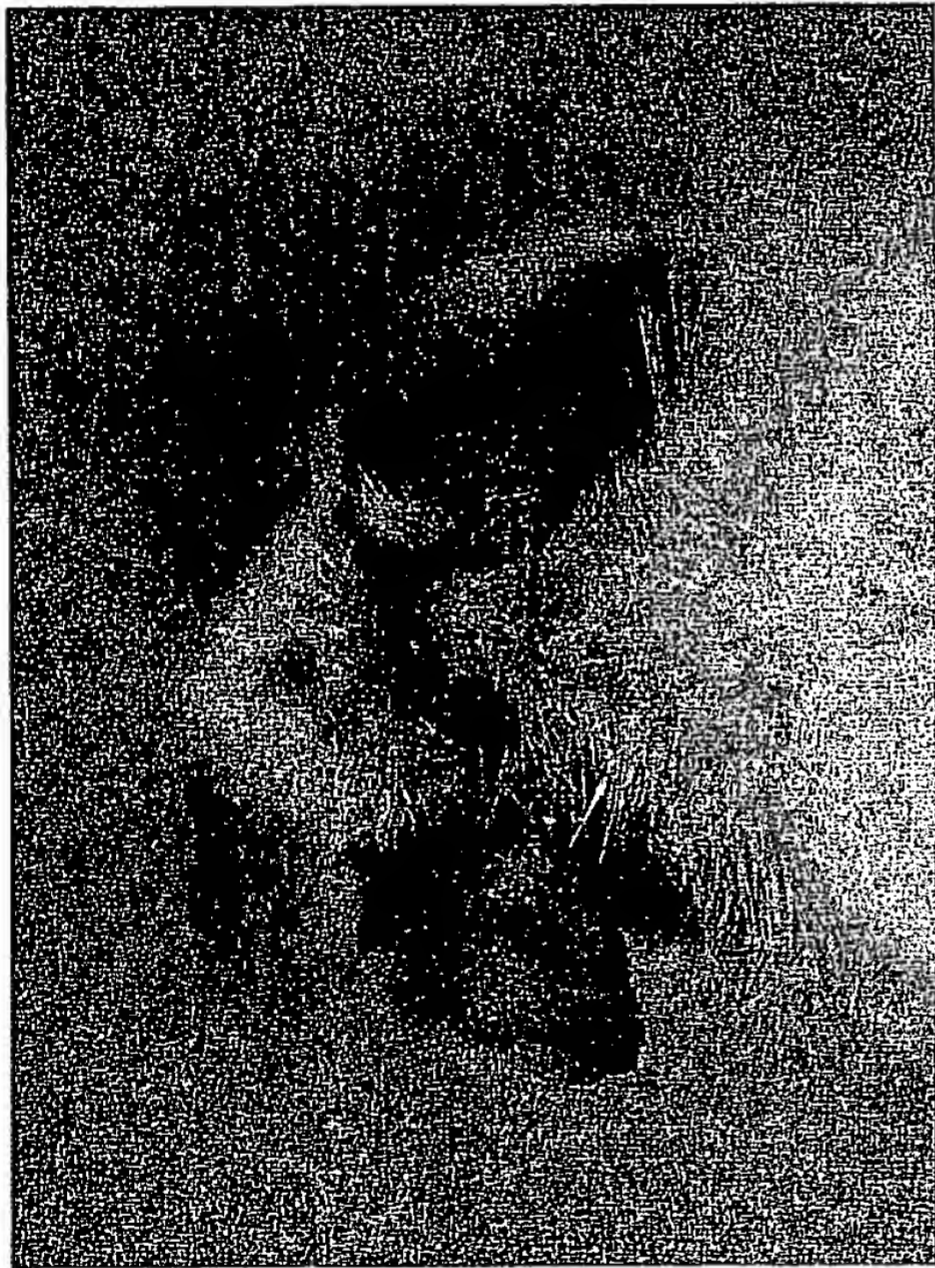


Fig.44 A-C

Fig.44A

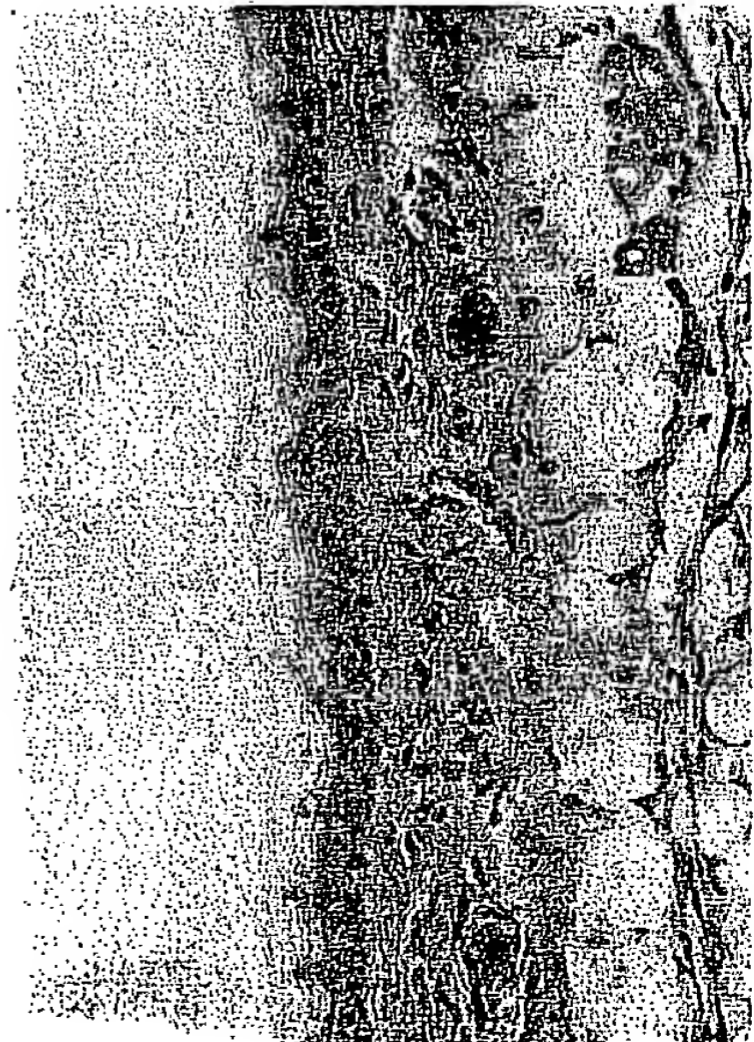


Fig.44B

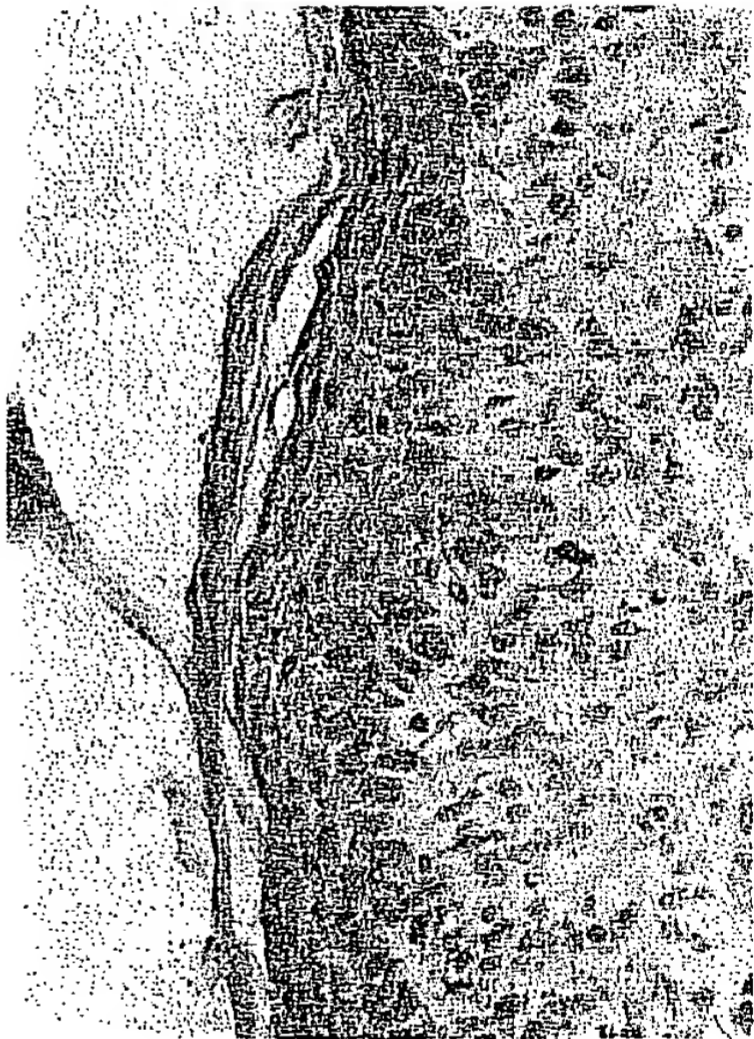


Fig.44C



Fig.45



Fig.46 A-B

Fig.46A



Fig.46B



FOOTED 223E2250

